Impact of *Foeniculum vulgare* Fortified Diet on Coagulation Profile and Some Biochemical Parameters

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Authors’ contributions

This work was carried out in collaboration among all authors. Author AA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author RI conceptualized, reviewed and edited. Author FH managed the analyses of the study. Author QUAB managed the literature searches. Author AA supervised. Author AA verified the analysis. All authors read and approved the final manuscript.

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ABSTRACT

**Aims:** Coagulation profile shows the clotting ability of blood. Biochemical tests indicate health status of vital organs such as liver, heart and kidneys. Herbal products are being assessed for their role in affecting these parameters. We evaluated role of *Foeniculum vulgare* incorporated diet on coagulation profile and some important biochemical parameters.

**Study Design:** Laboratory centred randomized controlled trial.

**Place and Duration of Study:** Pharmacology Department of University of Karachi, Karachi between June 2018 and September 2018.

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Methodology: After selecting 30 healthy rabbits of either sex, we placed them in three groups; Control, 2% *Foeniculum vulgare* and 4% *Foeniculum vulgare* group. Control group was given standard diet whereas; 2% and 4% *Foeniculum vulgare* groups were maintained on standard diet containing 2% and 4% *Foeniculum vulgare* crushed seeds. Coagulation profile and some biochemical parameters were done after interval of a month, for two months.

Results: Platelet count and fibrinogen increased while activated partial thromboplastin time (APTT) levels decreased in both the study groups animals as compared to control, while blood urea nitrogen (BUN), creatinine phosphokinase (CPK) and lactate dehydrogenase (LDH) elevation was noted both *Foeniculum vulgare* groups but within normal range.

Conclusion: *Foeniculum vulgare* may have some role in affecting coagulation and biochemical profile These parameters, however, need clinical trial to validate reliability.

Keywords: Activated partial thromboplastin time; blood urea nitrogen; creatinine phosphokinase; *Foeniculum vulgare*; lactate dehydrogenase.

1. INTRODUCTION

Coagulation disorder is usually presented with excessive bleeding as a symptom, especially as heavy menstrual flow in women [1]. This bleeding could be an indication of a bleeding disorder, thus, requires further investigation. Prevalence of bleeding vary according to various studies, though it is found to be a common symptom [2]. Platelet dysfunction (PDF) is thought to be a common cause of menorrhagia in women [3] could be up to 30% [4]. Fibrinogen is necessary for clot formation as well as platelets. Both these elements that is fibrinogen as well platelets count and function have a major role in coagulation disorders [5]. Creatinine levels and blood urea nitrogen are indicators of renal function [6]. Moreover elevated blood urea nitrogen could be an indicator of acute coronary syndrome [7]. The ratio of these two biochemical products of protein metabolism also point towards health status of heart failure patients [8,9]. Lactate dehydrogenase is an enzyme required for the conversion of pyruvate to lactate in anaerobic environment as well as indicator of liver function and it has some role in prognosis of various carcinomas in body [10-12]. Elevated creatinine phosphokinase level is indication of rhabdomyolysis [13]. Increase in levels of this biochemical parameter points towards injury to muscle membrane releasing myoglobin in blood which may negatively affect kidney function [14].

Herbal therapy has been proven of possessing protective role against elevation of the above mentioned biochemical parameters. The fennel (Botanical name: *Foeniculum vulgare* Mill, family Umbelliferae) is a known annual, biennial or perennial aromatic plant, according to the variety, has been well known since ages in Asia Minor, Europe and Mediterranean region. Almost all parts of this plant like fruits (seeds), leaves, and shoots are edible. *Foeniculum vulgare* fruits are oblong, curved or straight and are of greenish or yellowish brown colour. Volatile constituents of fennel seed consists of transanethole, fenchone, methylchavicol, limonene, α-pinene, camphene, β-pinene, β-myrcene, α-phellandrene, 3-carene, camphor, and cisanethole [15-17].

Aim of this study was to assess the effects of *Foeniculum vulgare* incorporated diet on coagulation profile and serum levels of some biochemical parameters.

2. MATERIALS AND METHODS

2.1 Study Design

This study was a laboratory centered randomized controlled trial conducted in the Pharmacology Department of University of Karachi. The ethical standards of the study were in line with the Interdisciplinary Principles and Guidelines for the Use of Animals in Research, Testing, and Education issued by the New York Academy of Sciences Adhoc Committee on Animal Research and the study protocol was approved by Board of Advanced Studies and Research (BASR), University of Karachi, Resol. No. 10(P)14 [16].

2.2 Herb Material

*Foeniculum vulgare* dried fruits were bought from a local departmental store and identified from the Pharmacognosy Department, Faculty of Pharmacy, and Pharmaceutical Sciences University of Karachi, and assigned voucher no. FVF-02-15/17.2.2 [17].

2.3 Animals

Thirty, healthy, adult, albino rabbits (weight 1500-2000 gram) belonging to either sex, were taken from the Animal house of Pharmacology.
department of University of Karachi. General health of all selected rabbits was checked during acclimatization period of a week, especially observing and noting for sign of diarrhea, hair loss, lack of activity and swelling. Animals were kept in transparent cages under controlled temperature of 23 ±2°C. Specific diet and water was provided ad libitum for 2 months. Rabbits were divided equally in 3 groups, Group 1 being the Control group, Group 2 (2% *Foeniculum vulgare*) and Group 3 (4% *Foeniculum vulgare*). Control rabbits were given standard diet, while, rabbits of group 2 and 3 were fed on 2% and 4% *Foeniculum vulgare* fruits incorporated diet, respectively.

### 2.4 Sample Collection

After a month’s interval 2 ml blood was collected twice, in K3-EDTA tubes for platelet count, and for coagulation profile blood was collected in test tubes containing 3.2% buffered trisodium citrate [18]. For estimation of prothrombin time standard reagent kits of Human Germany were used and analysed by Humaclot duo Coagulation analyser (Model no.18650, human Germany) [19,20]. Plasma fibrinogen estimation was done by employing hemostat fibrogen method (manual and automated determination of Plasminogen fibrinogen) as documented by Clauss [21]. The basis of this test is that 1:10 pre-diluted plasma thrombin is added in optimal quantity. Time taken by plasma to clot in the given sample has inverse relationship to concentration of fibrinogen [22]. Whereas, activated partial thromboplastin time (APTT) is conducted by adding an activating agent (phospholipid) and calcium to the citrated, platelet-poor plasma. The time to form fibrin clot was noted and the resulting value was matched either to the result of a normal control plasma sample done simultaneously, or to a normal value distribution [18,23].

### 2.5 Statistical Analysis

All values were statistically analyzed using SPSS 17.0. All readings were taken as mean±SD and compared by Analysis of variance (ANOVA) using post hoc Tukey’s test. P value = 0.05 was considered significant, P value = 0.01 was considered very significant and P value = 0.001 was considered as highly significant.

### 3. RESULTS

It is evident from results that platelet count increased in both *Foeniculum vulgare* fortified diets fed animals, while fibrinogen levels increased remarkably only in 4% *Foeniculum vulgare* group. In contrast APTT decreased in both study groups (Table 1).

Biochemical parameter assessment revealed slight lowering of serum creatinine levels while BUN values increased in both treated groups. Serum levels of CPK and LDH decreased in 2% *Foeniculum vulgare* group while increased in 4% *Foeniculum vulgare* group (Table 2).

### Table 1. Effect of *Foeniculum vulgare* diet in different ratio on coagulation profile

| Parameter | Groups | Day 30   | P value | Day 60   | P value |
|-----------|--------|----------|---------|----------|---------|
| Platelet Count (10^9/L) | Control group | 285.40±1.25 | 0.001<sup>a</sup> | 292.20±2.02 | 0.001<sup>a</sup> |
|          | 2% *Foeniculum vulgare* group | 341.99±2.28 | 0.001<sup>b</sup> | 794.47±1.71 | 0.001<sup>c</sup> |
|          | 4% *Foeniculum vulgare* group | 313.74±1.72<sup>1</sup> | 0.001<sup>a</sup> | 570.73±1.66 | 0.001<sup>a</sup> |
|          |        |          |         |          |         |
| Fibrinogen (g/L) | Control group | 2.3±1.19 | NS | 2.43±1.06 | NS |
|          | 2% *Foeniculum vulgare* group | 2.81±1.08 |         | 2.78±1.50 |         |
|          | 4% *Foeniculum vulgare* group | 4.05±1.41 | 0.009<sup>b</sup> | 3.35±1.30 | NS |
| Activated Partial Thromboplastin Time (seconds) | Control group | 34.78±1.36 | 0.01<sup>a</sup> | 34.39±3.32 | 0.01<sup>a</sup> |
|          | 2% *Foeniculum vulgare* group | 32.07±2.28 |         | 30.03±2.55 |         |
|          | 4% *Foeniculum vulgare* group | 23.22±1.20 | 0.001<sup>a</sup> | 28.54±1.4 | 0.001<sup>a</sup> |

<sup>1</sup>Values are mean ± SD, data analysed by one way ANOVA followed by multiple comparison (post hoc Tukey’s test)

<sup>a</sup>P-value in comparison to control

<sup>b</sup>P-value among the study groups

<sup>c</sup>P-value within the study group
Table 2. Effect of *Foeniculum vulgare* diet in different ratio on biochemical parameters

| Parameters                  | Groups                        | Day 30          | P-value | Day 60          | P-value |
|-----------------------------|-------------------------------|-----------------|---------|-----------------|---------|
| *Creatinine (mg/dl)*        | Control group                 | 1.07±0.67       | 0.110NS | 1.17±0.71       | 0.586NS |
|                             | 2% *Foeniculum vulgare* group | 0.77±0.12       |         | 0.84±0.11       |         |
|                             | 4% *Foeniculum vulgare* group | 0.72±0.16       | 0.051NS | 0.935NS         | 0.527NS |
| *Blood Urea Nitrogen (mg/dl)* | Control group                | 27.82±1.20      | 0.001   | 30.14±1.19      | 0.001a  |
|                             | 2% *Foeniculum vulgare* group | 39.62±2.61      |         | 35.35±1.24      | 0.001b  |
|                             | 4% *Foeniculum vulgare* group | 37.91±1.86      | 0.001   | 42±2.34         | 0.001a  |
|                             |                               |                 | 0.001c  |                 |         |
| *Creatinine Phosphokinase (mg/dl)* | Control group               | -               |         | 311.46±2.31     | 0.001a  |
|                             | 2% *Foeniculum vulgare* group | -               |         | 250.02±2.06     |         |
|                             | 4% *Foeniculum vulgare* group | -               |         | 542.78±2.17     | 0.001a  |
|                             |                               |                 |         |                 | 0.001b  |
| *Lactate dehydrogenase (mg/dl)* | Control group                | -               |         | 212.81±0.80     | 0.05a   |
|                             | 2% *Foeniculum vulgare* group | -               |         | 207.34±0.97     |         |
|                             | 4% *Foeniculum vulgare* group | -               |         | 251.81±0.26     | 0.001a  |
|                             |                               |                 |         |                 | 0.001b  |

10 Values are mean ± SD, data analysed by one way ANOVA followed by multiple comparison (post hoc Tukey’s test)

| P-value in comparison to control |
| P-value among the study groups  |
| P-value within the group        |

4. DISCUSSION

Blood coagulation profile is a basic criterion with respect to well-being of a patient. Hypercoagulability or hypocoagulability level in patient is a red sign. Thus, we assessed the impact of *Foeniculum vulgare* incorporated diet on coagulation profile in rabbits for two months.

This study showed significant elevation in platelet count of rabbits of both the treated groups which could be due to membrane stabilizing potential of *Foeniculum vulgare*. This is attributed to lowering of adverse effects caused by free radicals on cell membranes stability; therefore, elevation in cell count is noted. Change in fibrinogen levels was found to be insignificant except in 4% *Foeniculum vulgare* group which increased after a month.

Mansouri and colleagues noted in their study that, *Foeniculum vulgare* significantly elevated coagulation time [24]. Literature research revealed that compounds like coumarin, flavonoids, phenylpropanoid, and phenolic have anti-thrombotic and anti-platelet properties. Based on various trials, *Foeniculum vulgare* possess atypical composition, vasodilatory action and anti-platelet potential [25]. The phenylpropanoid compounds present in this herb exhibited the marked anti-platelet effect caused by inhibition of arachidonic acid and Thromboxane A and ADP [26].

Liver being the major organ of metabolism and detoxification has a basic role in converting various chemical compounds. As it is responsible for blood purification by transforming harmful compounds to harmless substances, it is also prone to injury by these toxic chemicals. The liver disorders are thought to be important health problems around the world. The conventional medical therapy is currently insufficient to handle this issue resulting in high morbidity and mortality. The drugs presently available for chronic liver disorders have unwanted effects [27]. Thus, studies are being conducted to find natural antioxidants possessing hepatoprotective action.

In this study serum lactate dehydrogenase levels were estimated for assessment of any toxic effects of *Foeniculum vulgare* containing diet in two ratios in rabbits. There was no significant difference noted among control and study groups indicating hepatic safety of this herb. An earlier study showed the hepatoprotective effect of *Foeniculum vulgare* against hepatotoxic agents such as diethyldithiocarbamate [28]. Another study documented that constituents such as D-
limonene and β-myrcene found in this herb elevate glutathione concentration in liver which is required by many enzymes that assist in formation of disulphide bonds of many proteins [29]. Hepatoprotective effects of *Foeniculum vulgare* could be attributed to its antioxidant potential and/or inhibitory effect on cytochrome and synthesis of oxon [30]. Devika and coworkers revealed the hepatoprotective impact of *Foeniculum vulgare* methanolic extract against paracetamol induced toxicity in rodents [31]. Similar study conducted by Ghanem et al revealed hepatoprotective potential of *Foeniculum vulgare* [32].

Nephrotoxicity is characterized by alterations in functions like inhibition of protein synthesis, decrease in glutathione depletion, lipid peroxidation and mitochondrial injury. Damage caused by oxidative stress is thought to be one of the major mechanisms leading to nearly all chronic nephrogenic pathologies [33]. Many herbs have been utilised for the treatment of kidney failure in traditional medicine around the world [34].

To assess renal function, serum creatinine, blood urea nitrogen and creatinine phosphokinase were estimated, in rabbits fed on 2% and 4% *Foeniculum vulgare* diet. Serum creatinine declined in both the treated groups as compared to control. A significant difference was noted with respect to BUN and creatinine phosphokinase in both study groups but the results of remained within the normal range. These findings suggest possible nephroprotective property of the study herb. Our results are in line with a study of El-Masry which demonstrated nephroprotective effect of *Foeniculum vulgare* against lead induced nephrotoxicity [35]. Similar renal protection was noted in another study using gentamicin as nephrotoxin and *Foeniculum vulgare* as protective agent [36]. Same effect was seen with 2% and 4% *Foeniculum vulgare* incorporated diet in our study.

5. CONCLUSION

The anticoagulant, hepatoprotective and nephroprotective actions noted in this study should be evaluated by clinical study as this herb could be a low cost alternative to presently available medicines.

CONSENT

It is not applicable.

ETHICAL APPROVAL

All authors hereby declare that "Principles of laboratory animal care" (NIH publication No. 85-23, revised 1985) were followed, as well as specific national laws where applicable. All experiments have been examined and approved by the appropriate ethics committee.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Friberg B, Kristin Örnö A, Lindgren A, Lethagen S. Bleeding disorders among young women: A population-based prevalence study. Acta obstetrician et gynecologica Scandinavica. 2006;85(2):200-206.
2. Sadler JE. Von Willebrand disease type 1: A diagnosis in search of a disease. Blood, The Journal of the American Society of Hematology. 2003;101(6):2089-2093.
3. Philipp CS, Dilley A, Miller CH, Evatt B, Baranwal A, Schwartz R, Bachmann G, Saidi P. Platelet functional defects in women with unexplained menorrhagia. Journal of Thrombosis and Haemostasis. 2003;1(3):477-484.
4. Kouides PA. Evaluation of abnormal bleeding in women. Current hematology reports. 2002;2(1):11-18.
5. Vij AG. Effect of prolonged stay at high altitude on platelet aggregation and fibrinogen levels. Platelets. 2009;20(6):421-427.
6. Narasimhan LR, Goodman W, Patel CKN. Correlation of breath ammonia with blood urea nitrogen and creatinine during hemodialysis. Proceedings of the National Academy of Sciences. 2001;98(8):4617-4621. Available:http://www.pnas.org/cgi/doi/10.1073/pnas.071057598
7. Saygitov RT, Glezer MG, Semakina SV. Blood urea nitrogen and creatinine levels at admission for mortality risk assessment in patients with acute coronary syndromes. Emergency Medicine Journal. 2010;27(2):105-109.
8. Matsue Y, van der Meer P, Damman K, Metra M, O’Connor CM, Ponikowski P, Teerlink JR, Cotter G, Davison B, Cleland JG, Givertz MM. Blood urea nitrogen-to-creatinine ratio in the general population and in patients with acute heart failure. Heart. 2017;103(6):407-413.

9. Brisco MA, Coca SG, Chen J, Owens AT, McCauley BD, Kimmel SE, Testani JM. Blood urea nitrogen/creatinine ratio identifies a high-risk but potentially reversible form of renal dysfunction in patients with decompensated heart failure. Circulation: Heart Failure. 2013;6(2):233-239. DOI: 10.1161/CIRCHEARTFAILURE.112.68230

10. Faloppi L, Scartozzi M, Bianconi M, Baroni GS, Toniutto P, Giampieri R, Del Prete M, De Minicis S, Bitetto D, Loretelli C, D’Anzeo M. The role of LDH serum levels in predicting global outcome in HCC patients treated with sorafenib: Implications for clinical management. BMC Cancer. 2014;14(1):110. Available:http://www.biomedcentral.com/1471-2407/14/110/prepubhttp://www.biomedcentral.com/1471-2407/14/110/prepub

11. Valvona CJ, Fillmore HL, Nunn PB, Pilkington GJ. The regulation and function of lactate dehydrogenase a: Therapeutic potential in brain tumor. Brain Pathology. 2016;26(1):3-17. DOI: 10.1111/bpa.12299

12. Wu SJ, Lin YX, Ye H, Xiong XZ, Li FY, Cheng NS. Prognostic value of alkaline phosphatase, gamma-glutamyl transpeptidase and lactate dehydrogenase in hepatocellular carcinoma patients treated with liver resection. International Journal of Surgery. 2016;36:143-151. DOI:https://doi.org/10.1016/j.ijsu.2016.10.033

13. Wool DB, Lemmens HJ, Brodsky JB, Solomon H, Chong KP, Morton JM. Intraoperative fluid replacement and postoperative creatine phosphokinase levels in laparoscopic bariatric patients. Obesity Surgery. 2010;20(6):698-701. DOI:https://doi.org/10.1007/s11695-010-0092-4

14. Landau M, Mesterman R, Ophir J, Mevorah B, Acalay J, Harel A, Nevo Y. Clinical significance of markedly elevated serum creatine kinase levels in patients with acne on isotretinoin. Acta dermato-venereologica. 2001;81(5).

15. Badgujar SB, Patel VV, Bandivdekar AH. Foeniculum vulgare Mill: A review of its botany, phytochemistry, pharmacology, contemporary application, and toxicology. BioMed Research International; 2014. DOI: http://dx.doi.org/10.1155/2014/842674

16. Abbass A, Ikram R, Khan SS, Ahmed S, Osama M. The Fennel, Foeniculum vulgare incorporated diet shows anxiolytic potential: A pre-clinical study. Pakistan Journal of Pharmaceutical Sciences. 2019;32(4):1813-9.

17. Abbass A, Ikram R, Hasan F, Adil A, Nisar U, ul Ain, Q. Antidepressant and Antiamnesic Potential of Foeniculum vulgare. Journal of Advances in Medicine and Medical Research. 2020;131-138. DOI: 10.9734/JAMMR/2020/v32i130360

18. Kamal AH, Tefferi A, Pruthi RK. How to interpret and pursue an abnormal prothrombin time, activated partial thromboplastin time, and bleeding time in adults. InMayo Clinic Proceedings 82.7, 864-873 Elsevier; 2007.

19. Davey FR, Fiske ML, Maltby A. Evaluation of a photoelectric automatic prothrombin analyzer. American Journal of Clinical Pathology. 1972;58(6):687-692. DOI:https://doi.org/10.1093/ajcp/58.6.687

20. Losner S, Volk BW, Jacobi M, Newhouse S. Photoelectric determination of prothrombin time. Translational Research. 1950;36(3):473-477. DOI:https://doi.org/10.5555/uri:pii:0022214350901892

21. Claus A. Rapid physiological coagulation method in determination of fibrinogen. Acta haematologica. 1957;17(4):237-246. DOI:https://doi.org/10.1159/000205234

22. Mackie IJ, Kitchen S, Machin SJ, Lowe GD. Haemostasis and Thrombosis Task Force of the British committee for standards in haematology, guidelines on fibrinogen assays. British Journal of Haematology. 2003;121(3):396-404.

23. Suchman AL, Griner PF. Diagnostic decision: Diagnostic uses of the activated partial thromboplastin time and prothrombin time. Annals of Internal Medicine. 1986;104(6):810-816.
24. Mansouri E, Kooti W, Bazvand M, Borooon MG, Amirzargar A, Afrisham R, Afzalzadeh MR, Ashtray-Larky D, Jalali N. The effect of hydro-alcoholic extract of *Foeniculum vulgare* Mill on leukocytes and hematological tests in male rats. Jundishapur Journal of Natural Pharmaceutical Products. 2015;10(1).

25. Tognolini M, Ballabeni V, Bertoni S, Bruni R, Impicciatore M, Barocelli E. Protective effect of *Foeniculum vulgare* essential oil and anethole in an experimental model of thrombosis. Pharmacological Research. 2007;56(3):254-260. DOI:10.1016/j.phrs.2007.07.002

26. Tognolini M, Barocelli E, Ballabeni V, Bruni R, Bianchi A, Chiavarini M, Impicciatore M. Comparative screening of plant essential oils: Phenylpropanoid moiety as basic core for antiplatelet activity. Life sciences. 2006;78(13):1419-1432. DOI:10.1016/j.lfs.2005.07.020

27. Bruck R, Hershkoviz R, Lider O, Aeed H, Zaider L, Matas Z, Barg J, Halpern Z. Inhibition of experimentally-induced liver cirrhosis in rats by a nonpeptidic mimic of the extracellular matrix-associated Arg-Gly-Asp epitope. Journal of hepatology. 1996;24(6):731-738. DOI:https://doi.org/10.1016/S0168-8278(96)80270-4

28. Kaneez FS, Hamdan AA, Hamza AE, Qadri SM. Protective effects of fennel extract (*Foeniculum vulgare* Mill.) on diethyldithiocarbamate-induced liver toxicity in rats. In The 7th Annual UAE, University Research Conference STD. 2005:91-97.

29. Helal EG, Eid FA, El Wahsh AM, Ahmed D. Effect of fennel (*Foeniculum vulgare*) on hyperlipidemic rats. The Egyptian Journal of Hospital Medicine. 2011;43(1):212-225. DOI:https://dx.doi.org/10.12816/efjm.2011.16779

30. Mansour SA, Heikal TM, Refaie AA, Mossa AH. Antihepatotoxic activity of fennel (*Foeniculum vulgare* Mill.) essential oil against chlorpyrifos-induced liver injury in rats. Glob J Environ Sci Technol. 2011;1(10).

31. Devika V, Mohandass S, Aiswary APR. Screening of methanolic extract of *Foeniculum vulgare* for hepatoprotective activity. Int J Pharm Pharm Sci. 2013;5(4):56-59.

32. Ghanem MT, Radwan HM, Mahdy ESM, Elkholy YM, Hassanein HD, Shahat AA. Phenolic compounds from *Foeniculum vulgare* (Subsp. *Piperitum*) (*Apiaceae*) herb and evaluation of hepatoprotective antioxidant activity. Pharmacognosy Research. 2012;4(2):104.

33. El-Ghany A, Ramadan AM, Ghozy SF. Nutraceutical effects of curcuma, ginger, celery, yeast and honey on side effects of gentamicin induced nephrotoxicity in rats. World Applied Sciences Journal. 2012;16(5):646-655.

34. Peesa JP. Nephroprotective potential of herbal medicines: A review. Asian Journal of Pharmacy and Technology. 2013;3(3):115-118.

35. El-Masry S, Ali HA, El Sheikh NM, Awad SM. Dose-dependent effect of coriander (*Coriandrum sativum* L.) and fennel (*Foeniculum vulgare* M.) on lead nephrotoxicity in rats. Int. J. Res. Stud. Biosci. 2016;4:36-45. DOI:http://dx.doi.org/10.20431/2349-0365.0406006

36. Shaheen U, Manzoor Z, Khaliq T, Kanwal T, Muhammad F, Hassan IJ, Mazhar H. Evaluation of nephroprotective effects of *Foeniculum vulgare* Mill, *Solanumnigrum* Linn. and their mixture against gentamicin-induced nephrotoxicity in albino rats. Int J Pharm Sci Rev Res. 2014;25(1):1-9.

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