

Knowledge and awareness of food and drug interactions (FDI): a survey among health care professionals

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ABSTRACT

Background: Most of the food and drug interactions (FDI) remain unnoticed and under reported due to either lack of proper history, follow up or unawareness. Certain foods and specific nutrients in foods, may affect the overall bio-availability, pharmacokinetics, pharmacodynamics and therapeutic efficacy of medications. FDI occur due to extension of drug action or due to interaction between the drug and herbal medicines as well as dietary supplements and food products.

Objectives: To evaluate the knowledge, attitude and awareness regarding the common FDI among the doctors in their day to day practice.

Materials and Methods: Survey included randomly selected 200 doctors divided into 3 groups [65 Professors, 83 Post Graduates (PGs) and 52 Interns] from JSS Tertiary care hospital, Mysore, India. Assessment was through FDI Questionnaire which consisted of 32 questions (included dichotomous, multiple choice and open ended questions). The differences between groups were compared using one-way ANOVA followed by Bonferroni's post-hoc test. The level of significance was set at $p < 0.05$.

Results: The mean scores (mean \pm SD) on the overall test were 26 ± 4.08 , 22.89 ± 3.72 , 21.35 ± 4.2 for professors, PGs and interns respectively, with 31 being a perfect score. Professors had good knowledge about FDI compared to others ($p < 0.001$). Only 33% participants have noticed FDI during their practice. A majority of doctors had heard, felt necessary to report and update their knowledge about FDI along with adequate patient counseling.

Conclusion: The study showed professors had better expertise compared to others. Intensive FDI training and integration of knowledge among healthcare professionals, especially in the younger health care professionals, is a requisite.

Key words: Drug interactions, food and drug interactions, questionnaire, adverse drug reactions.

Citation: Benni JM, Jayanthi MK, Tubaki BR, Renuka M. Knowledge and awareness of food and drug interactions (FDI): a survey among health care professionals. *Int J Pharmacol and Clin Sci* 2012;1:97-105.

INTRODUCTION

Interactions between the food and drugs can have profound influence on the compliance and success of drug treatment. In the health care setting, adverse drug reactions (ADR) and drug interactions (DI) present a growing concern. Several studies had shown the DI incidence ranging from 3% to 30%.^[1,2] Presence of additional drug, food, herbs, beverages or environmental chemicals alter the pharmacologic activity of a drug, leading to DI.^[3] A food-drug interaction is the effect of

food or a nutrient in food on the medications. Most of the people have an insight that being natural all herbs and foods are safe,^[4] but by altering, mainly the drug pharmacokinetics, they might cause ADR or oppose the effect of drugs.^[5-7] About one third of adults in the western world use herbal remedies with or

Received : 31 - 10 - 2012

Revised : 10 - 12 - 2012

Accepted : 17 - 12 - 2012

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Conflict of interest: Nil

Source of support : Nil

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without the notice of the treating physicians.^[8] Several studies have reported the evidence of interactions involving widely used herbs with prescribed drugs such as garlic and warfarin, St John's Wort and oral contraceptives.^[9]

High-risk patients taking three or more medications for chronic conditions like diabetes, hypertension, depression or congestive heart failure should be particularly monitored for FDI.^[10] Timing of food intake does affect the efficacy of certain medicines. Thus, food may either delay or decrease the absorption of the drug when taken with meals or some drugs are better tolerated when taken with food. Therefore, it's always advised to consult the physician regarding the timing of food consumption and the medicine.^[11] Doctors and pharmacists in every practice setting need to be vigilant and counsel the patients for potential FDI.

The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) have developed standards regarding drug - nutrient interactions and mandate healthcare professionals to counsel their patients on these interactions.^[12] FDI per se are very complex, varying in nature and there is a need for greater attention from the health care community. To investigate this type of interactions and alertness, we conceptualized this study with an objective to evaluate the knowledge, attitude and awareness regarding the common FDI among the doctors in their day to day practice.

MATERIALS AND METHODS

Study design:

The study was cross sectional, which included a newly designed structured, self-administered questionnaire which focused on common FDI mentioned in the medical literature. The validity of the items in a draft questionnaire were assessed by an expert panel

consisting of a pharmacologist, a registered dietitian and a physician, all of whom were educators in their respective fields. The panel validated the questionnaire for readability, question design, length and relevance. The items deemed uncommon in usual clinical practices were eliminated and some questions were revised to improve their clarity. A pilot study was done in a small group of subjects to assess the clarity and understanding of questions and then finalized. The study protocol was approved by the Institutional Ethics Committee.

Survey questionnaire:

A FDI Questionnaire (FDIQ) consisting of 32 questions (which included dichotomous, multiple choice & one open ended question), on the basis of FDI prevalence and importance, was used in this study (appendix 1). The FDIQ included dichotomous questions regarding food with relation to antihypertensive drugs, antithyroid drugs, antidepressants, anticoagulants, anti-retroviral therapy, peptic ulcer drugs and analgesics. Others included MCQs, counseling regarding FDI, any FDI noticed during their practice and one open ended question. The objective of one open ended question was to get suggestions, to incorporate the modifications and for the rigorous content validity of possible future revision of the questionnaires. The FDIQ also measured the participant's attitude towards the FDI.

Survey participants:

Present survey included randomly selected 200 doctors, divided into 3 groups [65 professors, 83 post graduates (PGs) and 52 Interns (house surgeons)] from JSS Tertiary care teaching hospital and Research Centre Mysore, Karnataka, India. Study was carried during the period July 2010 - August 2010 (2 months). Informed consent was obtained from all the participants before distribution of the

FDIQ. It took participants approximately 20 - 30 minutes to complete the survey form. The questionnaire did not reveal personal identity of a participant, recognized only the group. The answered questionnaires were collected and analyzed.

Statistical analysis:

Statistical analysis was carried out using SPSS Version 15.0. Results were expressed as mean \pm SD. Correct answers were given a value of one point and incorrect answers a value of zero point, maximum score was 31 points. Homogeneity of the data across the groups was evaluated by Pearson's Chi-square (χ^2) test followed by Mann-Whitney U test. The total score among different groups were compared using one-way Analysis of Variance (ANOVA) followed by Bonferroni's post-hoc test. The level of significance was set at $p < 0.05$.

RESULTS

The survey was completed within two months from the start of the study. Overall response rate was 100% and all completed the FDIQ within their stipulated time. The overall knowledge of the study participants was assessed based on their responses to the questionnaire. Table 1, displays the knowledge and comparison of FDIQ among professors, PGs and interns. Individual item values are expressed as percentage of correct answers in each group. The total scores of the overall test were; professors: 26 ± 4.08 , PGs: 22.89 ± 3.72 and interns: 21.35 ± 4.2 (Table 2). The one way ANOVA revealed that overall professors scored significantly ($p < 0.001$) higher than the PGs and interns. PGs scored better than interns, but was not statistically significant ($p > 0.05$). Most (98%) of the participants had heard of food and beverages interfering with drugs in the body. Professors

(100%), PGs (100%) and interns (94%) felt it is necessary to know about FDI and report them.

With relation to timings of food and drug intake, all group participants only knew about proton pump inhibitors (PPIs) and non-steroidal anti-inflammatory drugs (NSAIDs) but were not aware about the antidiabetic drugs like acarbose and glipizide (Q - 10c), antithyroid drugs (Q - 10e), antacids (Q - 10b) and isoniazid for tuberculosis (Q - 10b). Interns scored less regarding the common FDI like consumption of garlic or ginger with Coumadins (Q - 9e); dairy products with tetracyclines (Q - 9b); cheese, wine, beer and processed foods with MAO inhibitors (Q - 9c); alcohol with antihistamines (Q - 11c), etc as compared to other two groups. Only 66 (33%) participants had come across FDI during their clinical practice and 125 (62.5%) had not observed any. Professors had more frequently (Q - 18) noticed FDI as compared to the other groups. The common FDI noticed were theophylline with tea, tetracyclines with milk and metronidazole with alcohol in decreasing order of their occurrence during practice.

Most of the participants felt it is imperative to update one's knowledge on potential FDI every 3 to 6 months or every year so as to counsel the patients for effective therapeutics. The various ways to improve awareness regarding FDI suggested by the participants were: conducting continuing medical education (CMEs) on FDI, advertisements or banners in the OPDs, monthly institution newspapers, appointing a pharmacologist in the OPDs for counseling the patients, important FDI to be mentioned on the drug label, training pharmacists so as to counsel patients while dispensing medicines, development of a Food-Drug Counseling Center etc.

Table 1: Comparison of the knowledge of FDIQ in three groups (professors, PGs and interns): Expressed as percentage of respondents with correct answers for each questions

Q. no	Group I Professors (%) N= 65	Group II Post Graduates (%) N= 83	Group III Intern (%) N= 52	Pair wise comparison (p value)		
				Group I-II	Group I-III	Group II-III
1	98.5	98.8	98.1			
2	98.5	96.4	96.2			
3	100	100	94.2		0.03	0.029
4	100	97.6	94.2			
5	53.8	42.2	42.3			
6	95.4	90.4	86.5			
7	95.4	90.4	98.1			
8	72.3	83.1	78.8			
9a	96.9	89.2	94.2			
9b	93.8	78.3	73.1			0.041
9c	92.3	95.2	69.2		0.004	0.002
9d	89.2	77.1	76.9			
9e	76.9	56.6	38.5		0.006	
9f	46.2	38.6	46.2			
9g	80	43.4	46.2	0.012	0.025	
10a	96.9	95.2	94.2			
10b	76.9	66.3	46.2		0.035	
10c	64.6	37.8	48.1	0.009		
10d	83.1	85.5	71.2			
10e	70.8	49.4	46.2		0.008	
11a	92.3	80.7	75			
11b	83.1	59	50		0.009	
11c	86.2	73.5	73.1	0.025	0.029	
12	86.2	71.1	67.3			
13	78.5	57.8	61.5			
14	83.1	66.3	51.9		0.044	
15	98.5	85.5	78.8		0.029	
16	93.8	84.3	82.7			
17	87.7	78.3	73.1			
18	43.1	37.3	13.5		0.003	0.012
19	93.8	89.2	84.6			

Table 2: Total score, mean difference and the mean score percentage of knowledge on FDI among three groups

Total Score	Profes- sors (n=65)	Post Gradu- ates (PGs) (n=83)	Intern (n=52)
Mean \pm SD	26 \pm 4.08	22.89 \pm 3.72	21.35 \pm 4.20
Mean difference	- 5.0000	-8.1084	-9.6538
Mean score percentage	83.87%	73.84%	68.84%
p value	Profes- sors vs. PGs < 0.001	Professor vs. Intern < 0.001	PGs vs. Intern 0.087

Values are Expressed in Mean \pm Standard Deviation.

DISCUSSION

Our study was successful in evaluating the knowledge and awareness of FDI among doctors with varying degree of clinical experience. Our study revealed that professors were better in almost all the components of FDI than other groups which could be due to their higher periods of clinical learning and wide exposure through various CMEs, symposiums, conferences etc., but only 1/3rd had recorded FDI. Relatively, PGs with moderate clinical experience of 2-3 yrs had slightly better knowledge than the interns who had less than a year of experience.

Many problems in pharmacotherapy result due to drug interactions (DI).^[13] Drug interactions are consequences in which the effects of one drug are altered by prior or concurrent administration of another drug. The concept of DI is also extended to include: food drug interactions, herb drug interactions, laboratory drug interactions etc.^[13] Food and drug interactions might reveal more difficulties than a drug - drug interaction.^[14] Food induced changes in drug bioavailability determine the

majority of FDI and relate the clinical consequences of most of the drugs.^[15] Specific foods greatly affect drug therapy, resulting in serious side effects, or reduced absorption of a drug i.e. therapeutic failure^[16] or increase bioavailability.^[17] The clinical consequence of FDI depends on various factors like particular food consumed, drug dosage, herbs, patient's age and state of health.^[18] In the present scenario, drug approval occurs with increasing speed, therefore less information is available about a new drug ADRs and DI, as and when the drug reaches market.^[19] Various studies in the past have tried to evaluate the effect of food on drugs. Previous studies have reported gaps in the knowledge of physicians about the FDI.^[20, 21]

Both the PGs and interns scored less in certain fields of FDIQ like food and antihypertensive drugs, anticoagulants, antibiotics. Vitamin K rich food stuffs like broccoli, spinach and other green leafy vegetables promote blood clot formation and oppose the effects of the anticoagulants like warfarin, heparin, etc.^[22,23] A study showed deficiencies of the healthcare team with regard to warfarin-vitamin K interactions which can lead to disruption in anticoagulant outcomes.^[21] Similar deficiencies were seen in our study, PGs and interns had less information about vitamin K containing foods and their interaction with anticoagulants like warfarin. They were also not aware of interactions of dairy products with tetracyclines and fluoroquinolones, as earlier studies revealed tetracyclines to be taken one hour before or two hours after meals and avoided with milk as it forms insoluble chelates by binding with calcium and iron, affecting its bioavailability.^[24,25] Similarly casein and calcium present in milk decrease the absorption of ciprofloxacin.^[26,27] Previous studies have verified that, patients on anti-hypertensive drugs benefit from concomitant moderate sodium restricted diets^[28] and the

absorption of angiotensin converting enzyme inhibitors is increased when taken on an empty stomach.^[29,30]

In the present study, all doctors including professors had average performance in FDIQ with relation to timings of drugs and food intake. All were aware about NSAIDs and PPIs but lacked knowledge regarding the FDIs involving commonly used drugs like antidiabetics such as glipizide and acarbose, antithyroid, antacids, antiviral for HIV, isoniazid, etc. Earlier studies have shown that food greatly decreases isoniazid bioavailability,^[31] therefore must be taken on empty stomach in the early morning for maximum benefit. Glipizide, a sulfonylurea should be taken 30 minutes before meals.^[32] The maximum effectiveness of acarbose, an alpha-glucosidase inhibitor for diabetes is attained when the drug is taken just before ingesting the first portion of each meal.^[32] PPIs must be taken 30 minutes before breakfast as proton pumps are maximally active, than after meals.^[33] Food improves bioavailability of drugs like fenofibrate, mebendazole, isotretinoin, tamsulosin, carbamazepine, labetalol etc and fatty meal for griseofulvin.^[19]

Interns showed poor performance in overall FDIQ, which could be due to lack of knowledge, awareness and clinical exposure. Our study revealed that interns were not aware of cheese reaction. Cheese reaction is seen in depressive disorder patients on monoamine oxidase inhibitors (MAOIs).^[13,34,35] Interns also

lacked information regarding disulfiram like reaction with metronidazole.^[36] Among PGs and interns, PGs were slightly better though statistically non significant, probably due to their exposure and clinical experience than interns. Only one third doctors (n = 66), majority professors had recorded the FDI during their practice. The reasons for such low incidence among interns and PGs could be due to lack of awareness, clinical exposure or need of proper history and follow up of patients, etc.

Our results are similar to the previous studies^[20,21] who have also reported lack of knowledge about FDI among health care professionals. The outcomes of this survey showed that PGs' and interns' knowledge about the FDI was not satisfactory and only 1/3rd among all the study participants had recorded FDI during their clinical practice. Smaller sample size is one of the limitations of this study. Multicenter study with larger samples will be beneficial. Regional specificity of food, culture and even the individual specificity need to be considered. Therefore, additional training and integration of knowledge and expertise about FDI among healthcare professionals is needed to improve the therapeutic efficacy, patient's drug compliance and patient's safety.

ACKNOWLEDGEMENT

We sincerely thank the doctors of JSS Medical College and Hospital, Mysore, India, for their involvement in the study

Appendix:

Questionnaire used in this survey to assess the knowledge and awareness of food and drug interactions (FDI) among Health care professionals

Date:

Designation: Staff/ Intern / PG

Note: Please circle the appropriate option

- | | |
|---|----------|
| 1. Have you heard of food and beverage interfering with drug in the body? | Yes / No |
| 2. Food can speed up or slow down the action of a drug, do you agree? | Yes / No |
| 3. Is it necessary to know about the FDI? | Yes / No |

4. Is it necessary to report the FDI? Yes / No
5. Which age group of patients do you think are at a greater risk for FDI?
- a) <1 yr b) 1-4 yrs c) 5-14 yrs
- d) 15-45 yrs e) 46-59 yrs f) > 60 yrs
6. FDI: Includes food interacting with
- a) Diet b) Iron/ Vitamin supplements
- c) Alcohol and fruit juices d) All of the above
7. Impact of FDI depends on a various factors like drug dosage, person's age, & health status? Yes / No
8. At what level do the food/ beverages interfere with the drug commonly?
- a) Absorption b) Distribution
- c) Metabolism d) Excretion
9. Do you think that-
- a) A patient on drugs like theophylline / NSAIDs should avoid consuming large amount of tea, coffee & chocolates (Y / N)
- b) Avoid taking milk & dairy products, iron-rich food and supplements with tetracyclines and fluoroquinolones (Y / N)
- c) A patients on MAO Inhibitors should avoid cheese, processed meats, legumes , wine & beer, fava beans and fermented products (Y / N)
- d) Caffeine increases the risk of quinidine, diazepam, pseudoephedrine & theophylline drug toxicity (like nervousness, tremor, insomnia) (Y / N)
- e) Long period consumption of garlic/ginger along with coumarins should be avoided. (Y / N)
- f) Acidic foods and beverages-such as tomato sauce, tea, coffee, and citrus juices can be taken along with antibiotics (Y / N)
- g) Drugs like griseofulvin, ketoconazole and albendazole should be taken with fatty diet (Y/N)
10. With relation to timing of food intake, circle the correct option.
- a) Omeprazole / ranitidine, antihistamines- should be taken (before / with / after)
- b) Glipizide, isoniazid, antacids should be taken (before / with / after)
- c) Acarbose, voglibose should be taken (before / with / after)
- d) NSAIDs, steroids are advised (before / with / after)
- e) Thyroid hormones (before / with / after)
11. Alcohol and drug interactions
(Please mark x / √ in given brackets)
- a) Patients on drugs like metronidazole, cefaperazone, should avoid alcohol ()
- b) Food and milk decrease the absorption of alcohol and food increase the metabolism of alcohol ()
- c) Avoid taking alcoholic beverages with antihistamines ()
12. Food and Antihypertensive drugs
(Tick Correct Choice)
- a) Propranolol, ACE Inhibitors must be taken on empty stomach.
- b) Spironolactone must be avoided with potassium rich foods.
- c) Hypertensive patients require low salt diet.
- d) All are true
13. Food and ART drugs:
(Tick Correct Choice)
- a) Lopinavir / Ritonavir must be taken with food
- b) Didanosine and Indinavir must be taken on empty stomach
- c) Zidovudine can be taken without relation to food intake.
- d) All are true
14. Food and Anticoagulants:
Patients on Heparin / Warfarin should avoid foods like Spinach, broccoli, cauliflower , chick peas and pork in large quantities (Y / N)
15. Food and Antithyroid drugs:
A patient on thyroid supplements for hypothyroidism must avoid foods like Brussels, sprouts, turnips, cauliflower, millet and cabbage (Y / N)
16. Each patient require counseling regarding interactions of drug with food and beverages (Y/ N)

17. Which of the following information are important to the patients with respect to FDI?
- Read the prescription label on the container.
 - Read directions, warnings, interactions and precautions printed on all medication labels and package inserts.
 - Do not stir medication into your food or take capsules apart (unless directed by your physician).
 - Do not take vitamin pills at the same time you take medication.
 - Do not mix medication into hot drinks.
 - Never take medication with alcoholic drinks.
- g) All of the above
18. Have you come across any FDI? (Yes / No)
If so, mention type of Interaction _____
19. Is it imperative to update knowledge on potential FDI of medications, so as to counsel the patients? (Yes / No)
If so, how frequently _____
20. How can the awareness regarding the FDI be improved? Give suggestions.

REFERENCES

- Gosney M, Tallis R. Prescription of contraindicated and interacting drugs in elderly patients admitted to hospital. *Lancet* 1984; 2:564-7.
- Kinney EL. Expert system detection of drug interactions: results in consecutive inpatients. *Comput Biomed Res* 1986; 19:462-7.
- Baxter K, Davis M, Driver S, editors. *Stockly's Drug interaction*. Suffolk: Hodder and Stoughton by pharmaceutical press; 2000.
- Ismail MYM. Drug-food interactions and role of pharmacist. *Asian Journal of Pharmaceutical and Clinical Research* 2009;2:1-10.
- Fugh-Berman A. Herb - drug interactions. *Lancet* 2000;355:134-8.
- Huang SM, Hall SD, Watkins P, Love LA, Singh CS, Betz JM, et al. Drug interactions with herbal products and grape fruit juice: a conference report. *Clin Pharmacol Ther* 2004;75:1-12.
- Gohil KJ, Patel JA. Herb-drug interactions: A review and study based on assessment of clinical case reports in literature. *Ind J Pharmacol* 2007;39:129-39.
- Zhou S, Koh HL, Gaob Y, Gong ZY, Lee EJ. Herbal bioactivation: the good, the bad and the ugly. *Life Sci* 2004;74:935-68.
- Izzo AA, Ernst E. Interactions between herbal medicines and prescribed drugs: an updated systematic review. *Drugs* 2009;69:1777-98.
- D'Arcy PF. Nutrient-drug interactions. *Adverse Drug React Toxicol Rev* 1997;14:233-54.
- Williams L, Hill DP Jr, Davis JA, Lowenthal DT. The influence of food on the absorption and metabolism of drugs: an update. *Eur J Drug Metab Pharmacokinet* 1996;21:201-11.
- Joint Commission on Accreditation of Health Care Organizations: AMH provision for counseling about drug-food interaction. *JCAH Perspectives* 1986, 1994.
- Sharma HL, Sharma KK. Drug Interactions. In: *Principles of Pharmacology*. 1st ed. Hyderabad: Paras medical; 2007.p.945-51.
- Spence JD. Drug interactions with grapefruit juice: whose responsibility is it to warn the public?. *Clin Pharmacol Ther* 1997;61:395-400.
- Bushra R, Aslam N, Khan AY. Food-Drug Interactions. *Oman Med J* 2011;26:77-83.
- Aman SF, Hassan F, Naqvi BS, Hasan SM. Studies of food drug interactions. *Pak J Pharm Sci* 2010;23:313-20.
- Beermann B, Groschinsky-Grind M. Gastrointestinal absorption of hydrochlorothiazide enhanced by concomitant intake of food. *Eur J Clin Pharmacol* 1978;13:125-8.
- Hu Z, Yang X, Ho PC, Chan SY, Heng PW, Chan E, et al. Herb-drug interactions: a literature review. *Drugs* 2005; 65:1239-82.
- Bland SE, Vermeulen L. Drug-food interactions. *Journal of Pharmacy Society Wisconsin* 1998;Nov/Dec:28-35.

20. Lasswell AB, DeForge BR, Sobal J, Muncie HL, Michocki R. Family medicine resident's knowledge and attitudes about drug-nutrient interactions. *J Am Coll Nutr* 1995; 14:137-43.
21. Couris RR, Tataronis GR, Dallal GE, Blumberg JB, Dwyer JT. Assessment of healthcare professional's knowledge about warfarin-vitamin K drug-nutrient interactions. *J Am Coll Nutr* 2000;19:439-45.
22. Wells PS, Holbrook AM, Crowther NR, Hirsh J. Interactions of warfarin with drugs and food. *Ann Intern Med* 1994;121:676-83.
23. Booth SL, Charnley JM, Sadowski JA, Saltzman E, Bovill EG, Cushman M. Dietary vitamin K1 and stability of oral anticoagulation: proposal of a diet with constant vitamin K1 content. *Thromb Haemost* 1997; 77:504-9.
24. Gurley BJ, Hagan DW. Herbal and dietary supplement interactions with drugs. In: McCabe BJ, Frankel EH., Wolfe JJ editors. *Hand book of food-drug Interactions*. Florida: CRC Press; 2003.p.259-93.
25. Cardona Pera D. Drug-food interactions. *Nutr Hosp* 1999;14 Suppl 2:129S-140S.
26. Furedi P, Papai K, Budai M, Ludanyi K, Antal I, Klebovich I. In vivo effect of food on absorption of fluoroquinolones. *Acta Pharm Hung* 2009;79:81-7.
27. Papai K, Budai M, Ludanyi K, Antal I, Klebovich I. In vitro food-drug interaction study: Which milk component has a decreasing effect on the bioavailability of ciprofloxacin?. *J Pharm Biomed Anal* 2010;52:37-42.
28. Lacy CF, Armstrong LL, Goldman MP, Lance LL. *Drug interaction handbooks*. 13th ed. Ohio: Laxicomp; 2005.p.706-708.
29. Stormer FC, Reistad R, Alexander J. Glycyrrhizic acid in liquorice-evaluation of health hazard. *Food Chem Toxicol* 1993;31:303-12.
30. Mantyla R, Mannisto PT, Vuorela A, Sundberg S, Ottoila P. Impairment of captopril bioavailability by concomitant food and antacid intake. *Int J Clin Pharmacol Ther Toxicol* 1984;22:626-9.
31. Self TH, Chrisman CR, Baciewicz AM, Bronze MS. Isoniazid drug and food interactions. *Am J Med Sci* 1999;317:304-11.
32. Nolte MS. Pancreatic hormones and antidiabetic drugs. In: Katzung BG, Masters SB, Trevor AJ, editors. *Basic and clinical pharmacology*. 11th ed. New York: McGraw-Hill; 2009:p.727-47.
33. Sharma HL, Sharma KK. *Principles of Pharmacology*. 1st ed. Hyderabad: Paras medical publishers; 2007.p.386-99.
34. Rapaport MH, Thase ME. Translating the evidence on atypical depression into clinical practice. *J Clin Psychiatry* 2007;68:31-6.
35. Volz HP, Gleiter CH. Monoamine oxidase inhibitors. A perspective on their use in the elderly. *Drugs Aging* 1998;13:341-55.
36. Lieber CS. Mechanisms of ethanol drug-nutrition interactions. *J Toxicol Clin Toxicol* 1994;32:631-81.
