Assessment knowledge of food-drug interaction of academician population: Staff members, Students, and teaching assistants.

¹Obaid A. Alwan , Ahmaed A. Ashour², Marwan M. M. Almisawi³ Wafa M. Ateyyah⁴ , Maryam A. Alotairy⁵ and Haneen A. Alkamel⁶

¹,³Faculty members at the College of Medical Technology - Al-Zawia University.

² Department of Food Science and Technology- Faculty of Agriculture-University of Tripoli.

^{4,5,6} Clinical nutritionists

O.alwan@zu.edu.ly., a.ashur@uot.edu.ly, m.almisawi@zu.edu.ly

Abstract

Drug-food interactions can lead to a loss of therapeutic efficacy or the toxic effects of drug therapy. Therefore, this study is carried out to show the extent of knowledge regarding drug interactions. The study population included lecturers, teaching assistants, and students. A specially designed scientific questionnaire containing multiple questions was used. The results of this study showed that only 15% of pharmacists provide an explanation of drug interactions with food when they sell the medicine. Also, 26.67%, 15%, and 13.33% of students, lecturers, and teaching assistants, respectively, reported that they are interested in food development processes by following electronic scientific journals. On the other hand, the results indicate that 41.67%, 20%, and 13.33%, respectively, of students, lecturers, and teaching assistants have knowledge about the subject of drug-food

Key words: Drug, food, student, staff members, Illness, Therapy.

INTRODUCTION

Medications, both prescribed and over-the-counter, are used every day to treat acute and chronic illnesses. Drug-nutrient interaction is defined as an alteration of kinetics or dynamics of a drug or a nutritional element, or a compromise in nutritional status as a result of the addition of a drug [8]. Medications can help people live a healthy life for a prolonged period. Although medicines are prescribed often, it is important to realize that they must still be used with caution. Food becomes harmful to the body when it reacts with medications administered concomitantly in a diseased patient. Precisely a food-drug interaction is the result of a reaction between food and drugs [1]. The effect of food on drugs results in a reduction in the drug's bioavailability and alteration in drug clearance. On the other hand, Drugs can influence food intake, digestion, absorption and excretions [3]. Food and drug interactions play a significantly important role in the pharmaceutical field as they greatly impact the compliance and success of drug therapy. Food can affect one or all areas of pharmacokinetics, including absorption, distribution, metabolism, and elimination [18]. The ability of a natural product to interact with a drug is based on the same pharmacokinetic and pharmacodynamic principles as drug-drug interactions [4, 23]. The presence of an additional drug, food, herbs, beverages or environmental chemicals alters the pharmacologic activity of a drug, which may lead to disease [4]. The other methods for food-drug interaction include binding or chelation, altering gastric pH, altering gastrointestinal motility, or affecting transport proteins such as P-glycoprotein [41, 9, 30]. A food-drug interaction can: Reduce the therapeutic activity of a drug, cause a side effect from a medicine to get worse or better, cause a new side effect [10]. Defined by the Dietary Supplement Health and Education Act [24], dietary supplements include a wide array of nonfood, non-drug substances intended to supplement the diet, but are not intended to treat diseases or disorders of the human body [11]. These dietary supplements may also react in the body and produces food – drug interactions. Risk for food – drug interactions can be affected by many factors such as age, gender, medical co-morbidities, body composition, nutritional status, polypharmacy [13]. This questionnaire study includes some of the basic questions on the interaction of herbal and allopathic drugs, food and drug interaction and which age groups are highly susceptible to food-drug interaction.

Table 1. Examples of food – drug interactions

Food	Active constituent	Drug / Class	Effect
Milk products	Calcium	Tetracycline	tooth discoloration
Cranberry	Vitamin K	Warfarin and other anticoagulants	It increases the INR in patients on warfarin.
Coffee	Caffeine	Bronchodilators	Increases excitability and nervousness
Chocolate	Caffeine	Antidepressants	Decreases antidepressants activity
Banana	Potassium	ACE inhibitors	Increases potassium levels
Grapefruit	Furanocoumarins	Pshycotropics	Increases oral bioavailability
Alcoholic	Ethanol	Antiretrovirals	Toxic Epidermal Necrolysis, Hypersensitivity Syndrome
beverages			Reaction And Liver Failure.

Source : [5, 6].

Table 2. Allopathic-Ayurverdic interactions .

Herbs	Active constituent	Drug / Class	Interactions					
Aloe Vera	Anthraquinone glycosides	Digoxin and Thiazide	Increases cardiac toxicity					
Cranberry	Capsascin	Theophylin	May increase absorption					
Capsicum annum	Allicin	Antihypertensive Drugs	Herb may decrease BP					
Garlic (Allium sativum)	Caffeine	Antidepressants	Decreases antidepressants activity					
Ginko biloba	Ginkgolides	Anticonvulsants	Increases seizures					
Grapefruit	Furanocoumarins	Pshycotropics	Increases oral bioavailability, delay the absorption					
St. Johns wort	Hypericin and hyperforin	Oral contraceptives	Breakthrough bleeding, follicle growth and ovulation .					

Source: [5,11, 13, 22, 37].

Mineral supplements (magnesium, calcium, zinc, iron, selenium, iodine) need to be taken at least 2 hours away from antibiotics, as they can bind to the drug and reduce its absorption [24, 30]. Penicillin and erythromycin are destroyed by stomach acid when taken with food. So it is most effective when taken on an empty stomach. However, food can reduce the chance of stomach irritation from these drugs [7]. Food- drug interactions are equally important as drugdrug interactions, but are neglected due to less awareness and knowledge on it. The survey was carried out to determine the degree of awareness on food-drug interactions among College staff members of various departments, Lab technicians and Clinical nutrition students and medical laboratory students.

Methodology

A special scientific questionnaire was designed for this study, and it was carefully arranged and consists of two main areas: the first on general information For each member of the study community, and the second contains eight scientific questions related to the cognitive aspects of the drug and food interactions with the drug, in addition to other questions related to different scientific aspects. The spatial and temporal limits of this study are the College of Medical Technology - academic year 2017-2018. The study population included fourth-year students of clinical nutritional department, laboratory technicians and faculty members of the various departments in the college.

Coll Scientific question	naire for lect	cal Technology - ures , teaching a eraction between	ssistants and f	ourth year stud		oout the							
● First - general personal information Name (write the name as desired)													
Your work is: Teaching staff member Teaching assistant Student													
a) Have you ever it b) Did you know therapeutic benec c) When purchasi interaction with d) Do you follow Yes e) Are you follow f) What is the important g) Do you think the you have you think the processes: Yes	read about the that the interace of the drug ing medicines, some types of a newsletter or ing food development of this ce medicate educational fes No	did the pharmacis food: Yes Transcription Yes Transcription No Transcripti	a medicine and for with food leads of the standard provide you was a second provide you was a wareness will a second provide a wareness which was a waren	to the cancellation with sufficient info	ormation ortance to I goal: role in	about their							
Foods	Fruit juices	Grapefruit	spinach	Coffee	Fish	Dairy products							
Drugs	Drugs product												
Esomeprazole													
Theophylline													
Tetracycline													
Fexofenadine	neophylline tracycline cxofenadine												
Orlistat													
Phenelzine													
Antibiotics													

Figure (1) Model of study questionnaire

• Compilation and analysis of questionnaire data

The data obtained was analyzed using Excel 2007 to represent some of them in graphical models. We also used the statistical description to discuss the results of this study, which is as shown in the following:

About the general information for the study community

Survey data, showing that the female and male study population reached 108 and 21 persons respectively, including 98 students, 31 lecturers and laboratory technicians, with a percentage of 83.8% and 16%. The ages of the students ranged between 22 to 23 years, while the ages of the attendants and laboratory technicians ranged between 26 to 54 years.

About knowledge of dietary drug interactions

This axis includes eight questions, and we discuss this data, descriptively and graphically as in the following paragraphs:

• On the question (have you read about dietary food interactions).

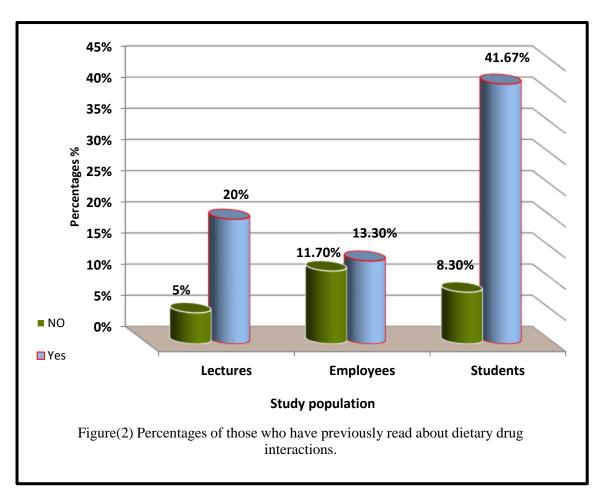
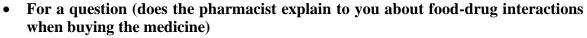
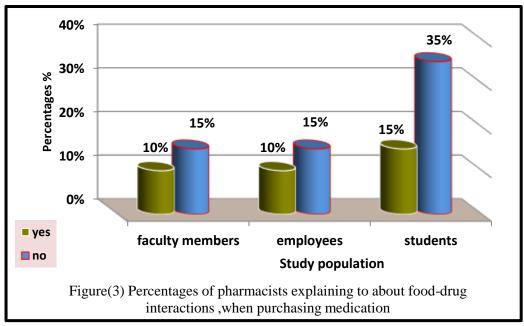


Figure (2) shows that 41.67% represented students who had already read about the interactions between food and medicine, while the percentage of lecturers was 20%. On the other hand, there is a convergence between the proportions of employees who have read and who have not read about food interactions and medicines, these employees are workers in the laboratories of the various scientific departments, also they hold a bachelor's degree in the fields of medical technology, and the ratios were 13.30% and 11.70%, respectively.

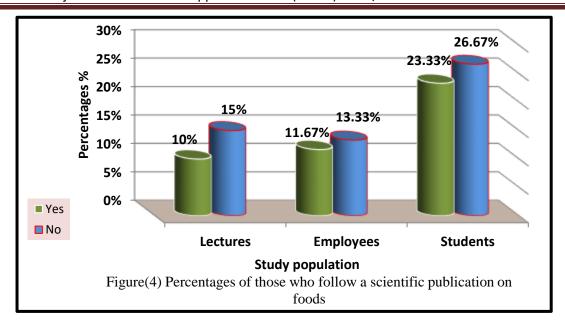


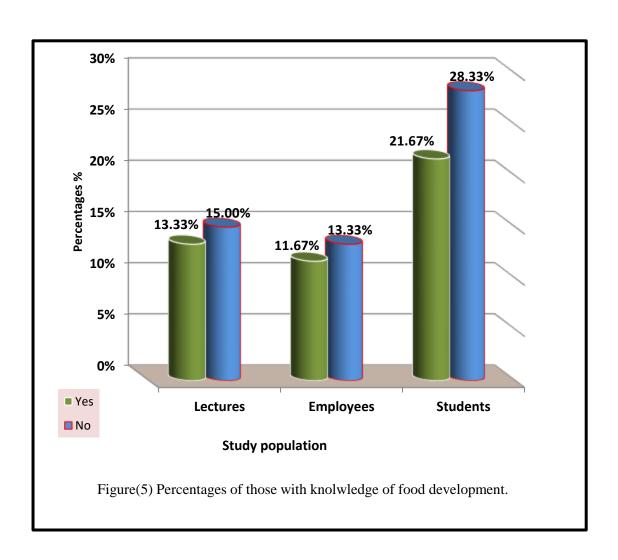


Figure(3) shows that 35%, 15%, and 15% of students, lecturers, and teaching assistants, respectively, indicated that when purchasing a pharmacist the pharmacist explains to them about drug interactions with foods. As for the largest percentage of the study population, which represents 85%, 85% and 65%, respectively, they indicated that the pharmacist does not provide them with any clarification on how to use the drugs, and they are satisfied with determining the dose and its times. Pharmacists who are not interested in providing the customer with explanations about medications, especially antibiotics, perhaps they are not graduates of the pharmacy college, or unaware of the seriousness of food interactions with the drug or they are indifferent, or that the client did not ask questions about the treatment and how to take it with food before or after it.

- For a question:- (If you are a follower of any scientific journal specialized in food science?)
- On the extent of knowledge of food development

Figure (4&5) shows that the percentage of students who follow the development of agricultural or industrial foods was only 21.67%, while it was lower among lecturers and Teaching Assistants 13.33% and 11.67%, respectively. On the other hand, it is clear that the percentage of those who did not know about food development was the highest and it has exceeded 53 % of the total study population





. This may be due to the absence of university libraries, and even if libraries are found, they are not supported by scientific journals related to food development. In our discussion with some of those who said that they knew about the development of food, we found that they depended on what some TV programs provide information about preparing food and serving it well

On knowing, which of the specific foods and drugs have interventions or side effect

Study population responses were categorized into two types of responses. The first is valid responses and the second is invalid responses. The questionnaire that does not carry any kind of responses was excluded. The percentage of each was calculated, and it is shown in Table (3) for the student group, while the results of Table (4) relate to the responses of lecturers and teaching assistants. Each table includes in the horizontal axis five types of foods commonly consumed by Libyan families, and in the vertical axis includes four types of medicines of different therapeutic purposes, in addition to the fifth column, which bears the general name of antibiotics. Some studies report that, an antibiotic is a type of antimicrobial substance active against bacteria and is the most important type of antibacterial agent for fighting bacterial infections. Antibiotic medications are widely used in the treatment and prevention of such infections, [15, 29, 30, 32, 36, 40]. The responses obtained from all members of the population of this study focused on the dairy and grapefruit category. Dairy products include milk as well as butter, yogurt, and cheese. After taking an antibiotic you may need to wait for up to three hours before eating or drinking any dairy products. Many studies have shown that most antibiotics that are taken orally may interfere with milk and dairy products, so it should be avoided taking them with these foods [2, 7, 18, 20, 28].

This study showed that the valid responses, which indicate the occurrence of interference between dairy products and antibiotics, were about 50% representing the student group and 54.8% representing the group of lecturers and teaching assistants, respectively, while the invalid responses were 30.6% and 32.3%, respectively. In the same context, Tetracyclines are a class of antibiotics, and our study showed that the percentage of valid and invalid responses about its interaction with dairy products was 41.8%, 42.9% and 29%, 71%, respectively. Also, the results of the two tables show that there are valid responses about the interaction between antibiotics and grapefruit (grapefruit juice or grapefruit slices), the percentage was about 38.8% for students and 42% of the lecturers and teaching assistants, while the invalid responses were about 34.7% and 58.1% respectively. There is no explanation for the invalid responses because the academic program for these students includes courses in pharmacology, plant food science, and animal source food in addition to clinical nutrition science, and the vocabulary of these courses includes lectures on drug interactions with foods, especially foods rich in calcium Like milk and dairy products such as yogurt and cheese, this interference occurs the upper part of the small intestine, which leads to delay or prevent the absorption of the drug, or the occurrence of side effects.

On the Phenelzine drugs: Phenelzine is a symptom used to treat symptoms of depression, as some studies have included its interaction with tyramine. Tyramine is a chemical found in foods and beverages such as aged, and fermented meats, Pickled herring, Broad bean pods and Aged cheeses, such as cheddar, English Stilton, Swiss, and blue cheese. In contrast, food that contains little or no tyramine such as Fresh meat, poultry, and fish, Cream cheese, Mozzarella, Ricotta cheese, Cottage cheese and Yogurt [12, 21, 35]. The percentage of responses valid for the interaction of Phenelzine with fish and dairy products was 35.7% for the student group and 33.7%, while the responses of lecturers and teaching assistants were 54.8% and 58.1%, respectively. On the other hand, the percentage of invalid responses was 54.1%, 52% and 45.2%, 42%, respectively.

Regarding the drug Fexofenadine, it is an antihistamine that is used to treat the symptoms of seasonal allergies (hay fever) in adults and children, [14]. Several studies suggest avoiding take fexofenadine with fruit juice (such as apple, orange, or grapefruit [28, 34].

The results of this study indicated that 36.7% of the students' responses indicated that they are fully aware of the presence of an interaction between Fexofenadine and fruit juice, as well as 39.7% of them know its interaction with grapefruit. While the invalid responses were 50% and 47%, respectively. Also, we find that 28.6% of responses that are not valid for students indicate that there are interactions between Fexofenadine and dairy products. On the other hand, the results show that the lecturers and repeaters have valid responses and invalid responses about the interactions of this drug with fruit juice and grapefruit, their percentage was about 51.6%, 71% and 48.4%, 35.5%, respectively.

On responses about the interferences of Orlistat with the types of foods indicated in the previous two tables, where several studies revealed that Orlistat (tetrahydrolipstatin) is a United States Food and Drug Administration (FDA) approved anti-obesity medication, and it is an inhibitor of pancreatic lipase. The result of this inhibition is that about 30% of the daily ingested fat intake is not absorbed.

This would lead to a 200-calorie deficit per day in an individual who consumed a diet of 2000 calories/day with 30% of calories as fat. [18, 19, 23]

Our study showed that 42.9% of students and 48.4% of lecturers and teaching assistants responded to avoiding taking Orlistat with El-bsaisah eaters, and they are considered valid responses. Whereas, the invalid responses were 41.8% and 32.3%, respectively. In addition, 22.4% of the students and 71% of the lecturers had invalid responses regarding the interactions between Orlistat and grapefruit. About Theophylline and its interactions with food, Mohammed, 2009 and Weinberger and Hendeles ,1996 have reported that, theophylline, is a drug used in therapy for respiratory diseases such as chronic obstructive pulmonary disease (COPD) and asthma.

Other studies indicate that Side effects from Theophylline drugs may get worse if you take too much Caffeine. Side effects may include nausea, irritability, nervousness, rapid heartbeat, tremors, or difficulty sleeping. Limit Caffeine intake while taking Theophylline. Drinking or eating foods high in caffeine, like coffee, tea, cocoa, and chocolate, may increase the side effects caused by theophylline. Avoid large amounts of these substances while you are taking theophylline. [2, 14, 17, 39]. The results obtained through the responses of the community of this study, showed that theophylline interferes with caffeine, and its percentage according to the responses of students and lecturers was about 30.6% and 35.5%, while the invalid responses were 63.3% and 45.2%, respectively.

About Esomeprazole drugs and its interference with foods, some studies have reported that, the primary uses of esomeprazole are gastroesophageal reflux disease, (GERD), this disease is a condition in which the digestive acid in the stomach comes in contact with the esophagus. The irritation caused by this disorder is known as heartburn. Esomeprazole reduces the production of digestive acids, thus reducing their effect on the esophagus. [16, 25, 26, 38].

Table (3) Percentage of valid and invalid student responses about the interaction of some drugs with the specific foods

Foods	oods Fruit juices			Grapefruit				El-besisa				Coffee				Fish					Dairy products			
Drugs	Invalid	Percentages	valid	Percentages	Invalid	Percentages	valid	Percentages	Invalid	Percentages	valid	Percentages	Invalid	Percentages	valid	Percentages	Invalid	Percentages	valid	Percentages	Invalid	Percentages	valid	Percentages
Esomeprazole	51	52	29	29.6					31	31.6	38	38.8	41	41.8	39	39.8					29	29.6		
Theophylline	25	25.5							19	19.4			62	63.3	30	30.6								
Tetracycline					34	34.7															41	41.8	42	42.9
Fexofenadine	49	50	36	36.7	46	47	37	39.7													28	28.6		
Orlistat					22	22.4			41	41.8	42	42.9									39	39.8		
Phenelzine	11	11.2															53	54.1	35	35.7	51	52	27	33.7
Antibiotics					34	34.7	38	38.8					27	27.6							30	30.6	50	51

Table (4) Percentage of valid and invalid lectures and lab technicians responses about the interaction of some drugs with the specific foods

Foods Drugs		Fruit juices				Grapefruit				El-besisa				Coffee				Fish				Dairy products			
	Invalid	Percentages	valid	Percentages	Invalid	Percentages	valid	Percentages	Invalid	Percentages	valid	Percentages	Invalid	Percentages	valid	Percentages	Invalid	Percentages	valid	Percentages	Invalid	Percentages	valid	Percentages	
Esomeprazole	19	61.3	11	35.5	18				17	54.8	9	29	13	42	15	48.4					12	38.7			
Theophylline	16	51.6	12	38.7	21				10	32.3	13	42	14	45.2	11	35.5									
Tetracycline					20	64.5															9	29	22	71	
Fexofenadine	15	48.4	16	51.6	11	35.5	22	71																	
Orlistat					22	71			10	32.3	15	48.4									23	74.2			
Phenelzine																	14	45.2	17	54.8	13	42	18	58.1	
Antibiotics					18	58.1	13	42					14	45.2							10	32.3	17	54.8	

The Most Common Acid-Reflux Triggers Include Citrus fruits, Peppermint, Caffeinated drinks (i.e. coffee and soda), Chocolate, Sugary foods, Spicy foods, Red and processed meats, Tomatoes and tomato-based products, High-fat or greasy (fried) foods, (Lind et al., 2000; Bobroff et al., 2009). In our study, the valid responses to students and lecturers, which indicated the presence of negative effects of carbazole with fruit juice, El-basaisa, and caffeine, came with a percentage of 29.6%, 38.8% 39.9% and 35.5%, 29% and 48.4%, respectively, while the response rate was Invalid 52%. 31.6%, 41.8% and 61.3%, 54.8% 42%, respectively.

About Esomeprazole and its interference with foods, some studies have reported that, the primary uses of esomeprazole are gastroesophageal reflux disease, (GERD), this disease is a condition in which the digestive acid in the stomach comes in contact with the esophagus. The irritation caused by this disorder is known as heartburn. Esomeprazole reduces the production of digestive acids, thus reducing their effect on the esophagus. [16, 25, 26, 31, 38]. The Most Common Acid-Reflux Triggers Include Citrus fruits, Peppermint, Caffeinated drinks (ie coffee and soda), Chocolate, Sugary foods, Spicy foods, Red and processed meats, Tomatoes and tomato-based products, High-fat or greasy (fried) foods, [7, 27]. In the present study, valid student responses and lecturer responses indicated negative effects of esomeprazole with fruit juice, El-besisa, and caffeine, with a percentage of 29.6%, 38.8% 39.9% and 35.5%, 29% and 48.4%, respectively, while the response rate was Invalid 52%. 31.6%, 41.8% and 61.3%, 54.8% 42%, respectively.

Other responses related to cultural media.

The responses of the study community members focused on the necessity of conducting health and food education through the implementation of studied scientific programs because the interaction between food medicines is one of the most important topics for every individual in the Libyan society. Most of the lecturers and all students indicated the necessity of intensifying awareness through audiovisual media.

Recommendations

This study recommends some points, which we consider to be of great importance, and include the following:

- Carrying out workshops on the topic of medical nutritional interaction, sponsored by specialized scientific colleges.
- Community awareness through audio and visual media.
- The establishment of a functional section on this subject, in the Ministry of Health and the Ministry of Information.
- Encouraging students in the near future to implement graduation projects, especially in aspects not covered in this study.
- Do not take vitamin pills at the same time you take medication. Vitamins and minerals can interact with some drugs.
- Do not mix medication into hot drinks because the heat from the drink may destroy the effectiveness of the drug

Conclusion

Food and drugs, both are necessary to maintain the health status of an individual. Regarding the parts of the field study, it appears that it includes the lecturers, teaching Assistants and Fourth-year students in the Clinical Nutrition Department and some medical laboratory students. Results indicate that 83.33% of students have already read some aspects of drug-food interactions. Also, 70% of them confirmed that the pharmacist sometimes when selling the drug cares about some clarifications about the interactions of this drug with some foods. Also,

53.33% of the total number of students followed some information about food in terms of food industry development and agricultural genetics and indicated the lectures they receive and what they found in social networks.

On the other hand, the results of this study showed that 60% of the faculty does not follow any scientific journal interested in food science. Some of them explained that there is no library in this college. Also 53.33% of technicians are not familiar with food development in both genetics and industrial. Our study points out some important recommendations that we consider necessary.

6. References

- 1- Adeneye AA, Olagunju IA . 2009. Preliminary hypoglycemic and hypolipidemic activities of the aqueous seed extract of Carica papaya Linn. in Wistar rats. Biol Med, 1:1–10.
- 2- Alvares, A. P., Anderson, K. E., Conney, A. H., and Kappas, A.: 1976. Interactions between nutritional factors and drug biotransformations in man, Proc. Natl. Acad. Sci. U.S.A. 73~2501.
- 3- Ayo JA, Agu H, Madaki I. 2005 . Food and drug interactions: its side effects. Nutr Food Sci; 35(4):243-252).
- 4- Ayrton A, Morgan P, .2001. Role of transport proteins in drug absorption, distribution and excretion. Xenobiotica 8: 469-497.
- 5- Berardini N, Fezer R, Conrad J, Beifuss U, Carle R, Schieber A .2005. Screening of mango (Mangifera indica L.) cultivars for their contents of flavonol O- and xanthone C-glycosides, anthocyanins, and pectin. J. Agric. Food Chem. 53: 1563-1570
- 6- Bergquist SA; Gertsson UE; Knuthsen P; Olsson ME. 2005. Flavonoids in baby spinach(Spinacia oleracea L.): changes during plant growth and storage. J. Agric. Food Chem. 53:9459-9464.
- 7- Bobroff B.L., Lentz A., Turner E.R., 2009 . Food/Drug and Drug/nutrient. Univ. florida IFAS, 4th ed:1-10.
- 8- Braun, L. 2012. An introduction to: drug-nutrient interactions. IMER Meet March, Monash Univ, pp.1-41.
- 9- Bushra R, Aslam N, Yar Khan A. Food-Drug Interactions. Oman Medical Journal, 2011; Vol. 26, No. 2: 77-83.
- 10- Cartea ME, Francisco M, Soengas P, Velasco P .2010. Phenolic compounds in Brassica vegetables. Molecules 16:251-280.
- 11- Chavez-Quintal P, Gonzalez-Flores T, Rodriguez-Buenfil I, Gallegos-Tintore S .2011. Antifungal Activity in Ethanolic Extracts of Carica papaya L. cv. Maradol Leaves and Seeds. Indian J Microbiol 51:54–60.
- 12- Chicago Dietetic Association. 2000. Manual of Clinical Dietetics. 6th ed. Chicago, IL: American Dietetic Association.
- 13- Christopher Owens, Tiffanie Toone, Michelle Steed-Ivie. 2014. A survey of dietary supplement knowledge, attitudes, and use in a rural population owens, J Nutr Food Sci.;4:5.
- 14- Compalati, E; Baena-Cagnani, R; Penagos, M; Badellino, H; Braido, F; Gómez, RM;
- Cornish, H. H., and Christman, A. A.: 1957. A study of the metabolism of theobromine, theophylline and caffeine in man, J. Biol. Chem. 228~315.
- 15- Del Rosso, JQ. 2009. Oral antibiotic drug interactions of clinical significance to dermatologists. Dermatol Clin.;27(1):91-94.
- 16- Dogra, H., Lad, B. and Sirisena, D., 2011. Paediatric gastro-oesophageal reflux disease. British Journal of Medical Practitioners, 4(2), pp.32-36.
- 17- Dubuis E, Wortley MA, Grace MS, Maher SA, Adcock JJ, et al. . 2014. Theophylline inhibits the cough reflex through a novel mechanism of action. J Allergy Clin Immunol 133: 1588-1598.

- 18- FAD. 2015. Avoid food drug interactions a guide from the national consumers league and Publication No. (FDA) CDER 10-1933.
- 19- Filippatos TD, Derdemezis CS, Gazi IF, Nakou ES, Mikhailidis DP, Elisaf MS. 2008. Orlistat-associated adverse effects and drug interactions: a critical review. Drug Saf. ;31(1):53-65.
- 20- Genser D (2008) Food and Drug Interaction: Consequences for the Nutrition/Health Status. Ann. Nutr. Metab. 52: 29-32.
- 21- Golwyn DH, Sevlie CP. 1996. Monoamine oxidase inhibitor hypertensive crisis headache: prevention and treatment. Headache Q Curr Treat Res.;7(3):207-214.
- 22- Hansten PD. (2004) Appendix II: important interactions and their mechanisms, In:
- 23- Jain SS, Ramanand SJ, Ramanand JB, Akat PB, Patwardhan MH, Joshi SR. Evaluation of efficacy and safety of orlistat in obese patients. Indian J Endocrinol Metab. 2011 Apr;15(2):99-104.
- 24- Joseph I. Boullata & Vincent T. Armenti . 2010. Handbook of drug-Nutrient Interaction Second Edition .Humana Press. USA.
- 25- Kahrilas, P.J., Shaheen, N.J. and Vaezi, M.F., 2008. American Gastroenterological Association Medical Position Statement on the management of gastroesophageal reflux disease. Gastroenterology, 135(4), pp.1383-1391
- 26- Li J, Zhao J, Hamer-Maansson JE, Andersson T, Fulmer R, Illueca M, Lundborg P. 2006. "Pharmacokinetic properties of esomeprazole in adolescent patients aged 12 to 17 years with symptoms of gastroesophageal reflux disease: A randomized, open-label study". Clin Ther. 28 (3): 419–27.
- 27- Lind, T., Rydberg, L., Kylebäck, A., Jonsson, A., Andersson, T., Hasselgren, G., Holmberg, J. and Röhss, K., 2000. Esomeprazole provides improved acid control vs. omeprazole In patients with symptoms of gastro-oesophageal reflux disease. Alimentary pharmacology & therapeutics, 14(7), pp.861-867.
- 28- Mohammed Yaheya , Mohammed Ismail .2009. Drug-Food interactions and role of pharmacist . Asian Journal of Pharmaceutical and Clinical Research (2) 4 :151-161
- 29- Novotni J. and Novotn2.1999. Adverse Drug Reactions to Antibiotics and Major Antibiotic Drug Interactions . Gen Physiol Biophys ,18: 126—139.
- 30- Otles S, Senturk A. 2014. Food and drug interactions: A general review. Acta Sci. Pol., Technol. Aliment. 13(1), 89-102.
- 31- Peter J. Barnes . 2013 . Theophylline. American J. of Respiratory and critical care medicine . Vol 188: 902 906 .
- 32- Piscitelli S, Rodvold K, Pai M. 2011 .Drug Interactions in Infectious Diseases. Third Edition. Springer New York Dordrecht Heidelberg London. Humana Press.
- 33- Reem Bassiouny Mahmoud El Lassy , Marwa Mohamed Ouda . 2019 . The Effect of Food-Drug Interactions Educational Program on Knowledge and Practices of Nurses Working at the Pediatric Out- Patients' Clinics in El-Beheira General Hospitals . Journal of Nursing and Health Science . 8(4): 34-48.
- 34- Shirasaka, Y; Mori T; Murata Y; Nakanishi T; Tamai I . 2014 . "Substrate- and Dose-Dependent Drug Interactions with Grapefruit Juice Caused by Multiple Binding Sites on OATP2B1". Pharm Res. 31 (8): 2035–2043.
- 35- Shulman KI, Walker SE, MacKenzie S, Knowles S. 1989. Dietary restriction, tyramine, and the use of monoamine oxidase inhibitors. J Clin Psychopharmacol.;9(6):397-402.
- 36- Stass H, Kubitza D. 2001 . Effects of dairy products on the oral bioavailability of moxifloxacin, a novel 8-methoxyfluoroquinolone, in healthy volunteers. Clin Pharmacokinet.;40(Supp 1):33–8.

- 37-Takanaga H, Ohnishi A, Yamada S, Matsuo H, Morimoto S, Shoyama Y, Ohtani H, Sawada Y .2000 . Polymethoxylated flavones in orange juice are inhibitors of P-glycoprotein but not cytochrome P450 3A4. J. Pharmacol. Exp. Ther. 293: 230-236.
- 38- Johnson, T.J. and Hedge, D.D., 2002. Esomeprazole: a clinical review. American journal of health-system pharmacy, 59(14), pp.1333-1339.
- 39- Weinberger M, Hendeles L. 1996. Theophylline in asthma. N Engl J Med; 334:1380–1388.
- 40- WHO . 1975. Requirements for Adverse Drug Reaction Reporting World Health Organization, Geneve, Switzerland.
- 41- Zhanel GG, Siemens S, Slayter K, Mandell L. 1999. Antibiotic and oral contraceptive drug interactions: Is there a need for concern? *Can J Infect Dis.*;10(6):429-433.