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QUALIFICATION WORK

on the topic: «PHARMACY STUDENTS' AWARENESS OF FOOD-DRUG INTERACTIONS»

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ANNOTATION

Irrational use of medicines is a major problem worldwide. Food-drug interactions may lead to loss of therapeutic efficacy, toxicity or therapeutic failure. Consideration of food-drug interaction helps to optimize pharmacotherapy. Therefore, pharmacists should advise patients on food-drug interactions. Knowledge of such interactions is crucial to avoid their occurrence. The master's thesis is devoted to the study of pharmacy student’s awareness regarding the main issues of the food-drug interaction. A questionnaire was developed, with the help of which a survey was conducted and the level of awareness of the respondents was assessed.

The total volume of the thesis is 50 pages, it consists of an introduction and 3 chapters and contains 4 tables, 7 figures, 55 references.

Keywords: food-drug interaction, diet, pharmacy students, awareness

АНОТАЦІЯ

Нераціональне використання ліків є великою проблемою в усьому світі. Взаємодія їжі та ліків може призвести до втрати терапевтичної ефективності, збільшення токсичності або терапевтичної невдачі. Врахування взаємодії їжі та ліків допомагає оптимізувати фармакотерапію. Тому фармацевти повинні консультувати пацієнтів щодо взаємодії їжі і ліків. Знання таких взаємодій має вирішальне значення, щоб уникнути їх прояву. Магістерська робота присвячена вивченню обізнаності студентів-фармацевтів щодо основних питань взаємодії лікарських засобів і їжі. Було розроблено анкету, за допомогою якої проведено опитування та оцінено рівень обізнаності респондентів.

Загальний обсяг дипломної роботи становить 50 сторінок, вона складається зі вступу та 3 розділів, містить 4 таблиці, 7 рисунків, 55 посилань.

Ключові слова: взаємодія ліків і їжі, харчування, студенти-фармацевти, обізнаність

LIST OF CONTENTS

ABBREVIATION LIST

AAG – α1-acid glycoprotein;

ACE – angiotensin-converting enzyme;

AUC – plasma concentration–time curve

BCRP – breast cancer resistance protein

BCS – Biopharmaceutics Classification System;

C_{max} – the maximal plasma drug concentration

CMs – chylomicrons;

CYP – cytochrome P_{450};

FDI – food-drug interaction;

GIT – gastrointestinal tract;

MAOI – monoamine oxidase inhibitors;

MRPs – multidrug resistance proteins;

OATPs – organic-anion-transporting polypeptides;

PD – pharmacodynamics, pharmacodynamic;

PD – pharmacokinetic, pharmacokinetics;

PEPT1 – peptide transporter 1;

P-gp – P-glycoprotein.

INTRODUCTION

Relevance of the topic. Irrational use of medicines is a major problem worldwide. World Health Organization estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately, and that half of all patients fail to take them correctly [1].

Drugs and food both play a role in disease prevention and treatment. In many disease conditions, dietary interventions are part of the overall therapeutic strategy. Patients need to consume proper food and nutrients, as well as safe and effective drugs. However, the combination of medicines and food can also lead to undesirable interactions that can impact therapeutic safety and efficacy. Food-drug interaction (FDI) is the result of a physical, chemical, or physiological relationship between a drug and food or nutrient. FDIs may affect the pharmacokinetics (absorption, distribution, metabolism, and excretion) or pharmacodynamic properties of a drug and can cause decreased or increased bioavailability of the drug resulting in treatment failure or adverse events.

Moreover, the influence of food on drugs depends on numerous variables, including the physicochemical properties of the drug, as well as enzymes and transporters present in the gastrointestinal tract. The presence and significance of drug-food interactions have been demonstrated by ample evidence. For instance, warfarin has been reported to interact with vitamin K-containing foods such as leafy green vegetables. Dietary vitamin K antagonizes the blood-thinning effect of warfarin, leading to unstable coagulation. Angiotensin-converting enzyme inhibitors or potassium-sparing diuretics (e.g., spironolactone) increase potassium levels in the body; thus, excessive consumption of salt substitutes and potassium-containing foods like bananas and oranges can lead to hyperkalemia. Foods containing high dietary fiber have also been shown to interact with the absorption of drugs such as levothyroxine and digoxin. Therefore, knowledge of drug-food interactions is essential to prevent these interactions.

The timing of food intake is an important factor that influences the occurrence of drug-food interactions. The presence of food may delay or reduce drug absorption, thus affecting the efficacy of such medicines. For example, the absorption of the antidiabetic drug glipizide is decreased in the presence of food and it is recommended that glipizide is taken on an empty stomach, 30 minutes before food. Thus, knowledge of the timing of food intake is also vital to achieve successful treatment and preventing adverse interactions [2-4].

Therefore, understanding the potential food-drug interactions and their mechanisms is crucial for healthcare professionals to ensure that patients receive optimal treatment.

As evidenced by the literature, several studies have already evaluated the knowledge of health professionals about FDI [2, 5-9]. However, no research has been conducted among pharmacy students in Ukraine, so we were interested in assessing pharmacy students' awareness.

The aim of the study – to evaluate the pharmacy students' awareness of food-drug interactions.

The objectives of the study:

1) analyze and summarize literature data on the mechanisms of drug-food interactions and the impact on the effectiveness and safety of pharmacotherapy.
2) develop an anonymous survey questionnaire to evaluate the pharmacy students' awareness of food-drug interactions.
3) conduct an anonymous survey of student pharmacists of NUPh using the developed questionnaire.
4) analyze the answers of the respondents and determine the level of the pharmacy students' awareness of food-drug interactions.

The study object – pharmacy students of the National University of Pharmacy.

5) **The study subject –** the level of the pharmacy students' awareness of food-drug interactions.

The research methods. Sociological (survey by questionnaire), system-analytical, statistical.

Practical significance of the obtained results. The obtained results substantiate the expediency of familiarizing practicing pharmacists and students of special pharmaceutical education with the influence of food-drug interactions on the effectiveness and safety of pharmacotherapy. Research results can be considered when revising educational and professional programs and improving the content of educational components.

Approbation of research results and publications. Abstract was published based on the results of the work: Bourrous Ahlam, Scientific supervisor: Stepanova S.I. Pharmacy students' awareness of food-drug interactions: Topical issues of new medicines development: Materials of II XXIX International scientific and practical conference of young scientists and students (April 19-21, 2023, Kharkiv). – Kharkiv: NUPh, 2023. P. 367-368.

Structure and volume. The qualification work contains an introduction, the literature review, 2 chapters of the experimental part, conclusions, and a references list of used (55 literature sources). The volume of the main text of the work is 50 pages. The work is illustrated with 4 tables and 7 figures.

CHAPTER 1
THE PROBLEM OF FOOD-DRUG INTERACTIONS TO ENSURE SUCCESSFUL PHARMACOTHERAPY (LITERATURE REVIEW)

1.1. Pharmacological mechanisms of food-drug interactions

FDI is the consequence of a physical, chemical, or physiological relationship between a drug and substances present in food or dietary supplements. Among the many different factors that can affect the therapeutic efficacy of drugs, food occupies an important place. The problem of FDI has several aspects, the main of which are: the influence of food components on the therapeutic drug effectiveness; the influence of food components on the toxicity of drugs; the influence of drugs on the physiological processes of digestion; the influence of drugs on the occurrence of pathology of the digestive system; clinical and pharmaceutical aspects of the use of dietary supplements; replenishment of nutrient missing in food (vitamins, microelements, proteins, amino acids, essential fatty acids, etc.); medical treatment of diseases caused by food products [3, 10].

The most frequently, FDI occurs during the enteral administration of drugs. But the interaction can take place with intramuscular, intravenous, transdermal, inhalation and other parenteral routes of administration of the drug. The nature of the diet has the greatest effect on systemic drugs, but there are cases when even local medicines change their effect under the influence of food or drugs affect the digestive process [11].

FDI is impacted by plenty of factors, like physicochemical nature, size and molecular weight of the compounds, etc. Also, the dosage form of the drug and/or excipients included in its composition can significantly affect it. However, it is impossible to accurately predict FDI only based on physicochemical properties of drugs [12]. The development of FDI may depend on the composition of food, as well as on a certain time of taking drugs in relation to food [13].

Medications interact with foods and nutrients in several ways. Food-drug interactions can be broadly classified as occurring at (I) pharmaceutical (compatibility, solubility, stability), (II) pharmacokinetic (absorption, distribution, metabolism, excretion), or (III) pharmacodynamic (clinical effect) level, and are the result of physical or chemical exchanges between a food molecule and a drug. Understanding the mechanisms by which the dietary substances alter drug PK and PD outcomes is critical to assess clinical significance and management. Whereas pharmacokinetic (PK) food-drug interactions can have a variety of causes, pharmacodynamic (PD) food-drug interactions occur due to specific pharmacological interactions between a drug and particular food. PK interactions are the most common and well-studied [5, 14].

1.1.1. Pharmacokinetic interactions

The various stages in which food can interact with a co-administered drug occur during absorption, distribution, metabolism and elimination. metabolism and elimination.

The PK mechanisms have been elucidated. Their occurrence depends mainly on the properties of the medicinal substance, the composition of the dosage form and several physiological factors. Each meal changes the physiological conditions in the gastrointestinal tract (GI) of a person, so it can affect the drug PK [15].

Fisher et al. reported that FDI could generally be predicted based on the Biopharmaceutics Classification System (BCS). According to BCS, drugs are classified into four categories based on their solubility and intestinal permeability. Class 1 drugs with high solubility/high permeability; high-fat meal will have no significant effect on drug bioavailability, Class 2 drugs with low solubility/high permeability; high-fat meal will increase drug bioavailability, Class 3 drugs with high solubility/low permeability; high-fat meal will decrease drug bioavailability, Class 4 drugs with low solubility-low permeability; it is difficult to predict what will

occur (table 1.1) [6, 7]. Gu CH et al. further improved the prediction of food effects by classifying drugs based on solubility, permeability and dose of a compound [16].

Table 1.1

Biopharmaceutics classification system classes and metabolism of drugs

Metabolism	BCS class, preparations		BCS class, preparations	
	High solubility		Low solubility	
Extensive	I. high permeability	propranolol, theophylline, zidovudine	II. high permeability	carbamazepine, celecoxib, ketoconazole
Poor	III. low permeability	cimetidine, trospium, atenolol	IV. low permeability	nelfinavir, venetoclax, furosemide

Thus, with high fat food, the bioavailability of lipophilic lipids (albendazole, griseofulvin) often increases due to increased solubility of lipids or stimulation of bile secretion. On the contrary, a high fiber content in the diet can reduce the bioavailability of some drugs (digoxin, lovastatin) due to binding with fiber. However, these conditions are often understudied [17].

1.1.1.1. Food effect on drug absorption

Orally administered drug absorption is determined by its physicochemical properties, formulation, the capability of transportation (active or passive) across epithelial cells in the GIT and the administration during fasted/fed state [18].

It is well known that food influences drug absorption by delaying gastric emptying time, altering the pH of the gastrointestinal tract, stimulating bile flow, increasing splanchnic blood flow, or physically interacting with drugs. In addition, different foods, depending on the nutritional composition (rich in proteins, carbohydrates or fats), calories, volume, temperature and fluid intake, have different effects on transit time, dissolution in the lumen, permeability and bioavailability of the drug [16].

After physical and chemical processing in the oral cavity and stomach, the food eaten enters the intestines, where it is absorbed and partially metabolized. The transport of any molecules through biological membranes (including food products and drugs) can occur through passive (along the concentration gradient, without energy consumption) or active (with the help of carrier proteins, with energy consumption) transport. Since the same pathways and transporter proteins are used for the absorption of drug and food molecules, the interaction of food and drugs due to competition is inevitable [15, 19].

At the level of absorption, food-drug interactions can be classified into 5 categories: those causing reduced, delayed, increased and accelerated drug absorption, and those in which food has no effect. Decreased drug absorption can be due to drug instability in gastric fluids, complexation interactions (e.g. between drugs and metal ions or dairy products), binding to dietary compounds (pectins, fibers) and increased viscosity of the luminal content. Delayed drug absorption can be a result of a slower gastric emptying rate or increased gastric pH resulting from the ingestion of food (e.g. weakly basic drugs have slower dissolution rates at higher pH). The intestinal uptake of poorly soluble drugs can be increased by the food intake as a result of the secretion of bile salts [20].

Adsorption can be passive (by concentration gradient) or active (by transporters). Enterocytes have a variety of transporters and enzymes specialized in the absorption, excretion, and metabolism of a variety of nutrients. FDI often occurs in the case of competition for the same transport route

The list of known absorption and excretion transporters in the human intestine (and other organs) is quite extensive [17, 21]. Because of multidrug transporters, the drug efficacy can vary from patient to patient. A dose that might be effective for one individual may be toxic for another individual and it is also highly possible that the drug may have no effect at all [22].

Organic anion transporting polypeptides (OATPs) are important transporter proteins. OATP transporters are involved in the transport of endogenous and exogenous substrates, including bile acids, thyroid hormones, prostaglandins,

bilirubin glucuronides and many clinically important drugs such as statins, protease inhibitors, fexofenadine, midazolam, montelukast, aliskiren and talinolol. OATP1A2, OATP2B1, OATP1B1 and OATP1B3 are the most important OATP isoforms and influence the pharmacokinetic performance of drugs. OATP2B1 is believed to be actively involved in the absorption of nutrients and drugs from the human GIT. The co-administration of drugs or other molecules that compete with specific OATP isoforms has the potential to elicit pharmacokinetic interactions. Unexpected adverse effects may occur if a conventional drug with a narrow therapeutic index competes for specific OATPs with herb/food chemicals. For instance, the consumption of fruit juices such as grapefruit, apple and orange juice, can significantly reduce the oral bioavailability of drugs due to the inhibition of intestinal OATPs. *In vivo* studies in patients have suggested that co-administration of grapefruit, orange or apple juices decreased the systemic availability of fexofenadine by 65–75% and celiprolol by more than 80%, due to reversible inhibition of intestinal OATP. Fruit juices that contain high concentrations of naringin directly inhibit enteric OATP1A2 and decreas the oral bioavailability of fexofenadine. Catechins and polyhydroxylated flavonoids such as theaflavin, that are present in tea can impact on OATPs and reduce systemic exposure to OATP drug substrates like rosuvastatin [15, 23]. Epigallocatechin and epicatechin that are present in green tea both at 100 μM inhibited OATP2B1-mediated estrone-3-sulfate uptake by ~70%. Epigallocatechin at at 100 μM also inhibited OATP1A2-mediated estrone-3-sulfate uptake by ~75%. The consumption of a cup of GT (e. g., 240-300 ml) will result in the inhibition of OATP activity due to high concentrations of catechins in the intestinal line [24].

Clinical data on food-drug interactions showed that the flavonoid quercetin significantly reduced the bioavailability of pravastatin (an OATP1B1 substrate), grapefruit, orange and apple juice reduced the bioavailability of fexofenadine, orange juice reduced the C_{max} and AUC of atenolol (an OATP1A2 and 2B1 substrate), grapefruit juice reduced the C_{max} acebutolol (an OATP1A2 substrate),

green tea reduced the absorption of rosuvastatin and nadolol due to inhibition of OATP1A2 and OATP2B1-mediated intestinal uptake of the drug [25].

Oligopeptide transporters (peptide transporter 1 – PEPT1) are mainly located in the apical membranes of intestinal epithelial cells and are responsible for the bioavailability of various drugs. The most common substrates are L-dopa, β-lactam antibiotics and some angiotensin-converting enzyme (ACE) inhibitors [26, 27]. The interaction can occur when the oligopeptide competes with peptide medicine. Thus, it was shown that the treatment of Parkinson's disease with levodopa was more effective when following a low-protein diet [15, 26]. Also, it was reported that fasting increases the transcription of PEPT1 in experimental animals, which theoretically implies an increase in the absorption of peptide drugs [27].

P-glycoprotein (P-gp, ABCB1- protein) is the most studied membrane efflux transporter, which is involved in the transport of endogenous and exogenous substrates from cells to the extracellular space and biological fluids. P-gp is present in various tissues of the body, including the brain, kidneys, liver, GIT, testis and placenta, but in the intestine, it causes a number of clinically significant FDIs [22].

Possible mechanisms by which food can interact with P-gp include downregulation of intestinal P-gp expression, competitive inhibition with other P-gp substrates and alteration of the membrane fluidity [20].

As many compounds can influence intestinal metabolic activity, this effect is also noted for several food compounds having a modulatory effect on P-gp. A wide spectrum of its substrates has been identified, including antiarrhythmic, antihypertensive drugs, cyclosporine, tacrolimus, and morphine. The main food inhibitors of P-gp are furanocoumarins and flavonoids present in fruits and vegetables. The *in vitro* data suggest that the flavonoids and furanocoumarins present in grapefruit juice can inhibit the P-gp activity modifying the disposition of drugs that are P-gp substrates such as talinolol [15, 21, 28]. Co-administration with food components that have an inhibitory effect on intestinal P-gp might indeed be a simple and safe strategy to increase the oral absorption of P-gp substrates [29].

Extracts of St John's wort (*Hypericum perforatum* L.), used in the treatment of depression as an over-the-counter drug, induced P-gp transporter activity in the GIT after chronic treatment. In a placebo-controlled parallel study, it was shown that the plasma area under the curve (AUC) of digoxin decreased by 25% after ten days of treatment with hypericum extract. Co-administration of hypericum extract decreased indinavir AUC by 57%. Acute heart and kidney transplant rejection due to decreased ciclosporin levels (reduction of more than 50%) with co-administration of St John's wort has been reported in several case studies. *In vitro* analysis revealed that P-gp and CYP3A4 could be induced at low, clinically relevant concentrations of St John's wort and hypericine [20].

There are other transporters of substrates from cells to the extracellular space and body fluids, including multidrug resistance-associated proteins (MRPs) and breast cancer resistance protein (BCRP). MRPs release conjugated metabolites of glutathione, glucuronides or sulfates from the enterocyte. Flavonoids are inhibitors of these transporters. Thus, phase II metabolites of quercetin (especially glucuronides) are potent inhibitors of MRPs in vitro. Similarly, BCRP expressed in the apical membrane of intestinal cells transports conjugated metabolites including statins, steroid hormones, folic acid, and vitamins B_2 and K_3. This suggests a possible FDI due to effects on these transporters [15, 30, 31].

Molecules that increase the intestinal monolayer fluidity may theoretically affect drug absorption, as increased fluidity may increase the rate of diffusion of some drugs. Flavonoids, cholesterol, and α-tocopherol have been shown to increase the fluidity of cell membranes. However, these *in vitro* results have not yet been clinically proven [15, 31].

The absorption of oral drugs can be influenced by the simultaneous introduction of food, which leads to undesirable interactions caused by the inhibition or induction of intestinal metabolism enzymes.

CYP3A and CYP2C9 account for more than 95% of all cytochromes P450 in the intestine. Intestinal metabolism with the participation of CYP3A contributes to the first-pass effect of many drugs, such as cyclosporine, verapamil, felodipine,

midazolam, tacrolimus, simvastatin and nifedipine. Metabolism can be enhanced by inducers of these enzymes, such as hyperforin (St. John's wort), which can result in dramatically reduced oral drug absorption and a threatened drug efficacy [32].

Clinical studies have shown that citrus juices, including grapefruit juice, increase the bioavailability of drugs that are CYP3A substrates by inhibiting these intestine enzymes. The effect was long-lasting, as a completely new de novo synthesis is required to restore enzymatic activity. The degree of food influence on the activity of metabolizing enzymes and intestinal transporters varies greatly from person to person [15, 19].

A well-known example of a specific food-drug interaction is the formation of stable chelate complexes with divalent metal cations, such as calcium or magnesium, which are widely present in many foods. The chemical structure of chelating agents can easily explain the reasons for complex formation. Tetracyclines and quinolones have been shown to form complexes with food cations or antacids, reducing drug absorption [15].

As can be seen from the above review of the literature, food causes numerous changes in the gastrointestinal tract, which can increase, decrease, slow down or accelerate the intestinal absorption of the drug depending on the properties of the drug.

1.1.1.2. Food effect on drug distribution

Drug distribution means the reversible transfer of a drug from the blood to organs through vascular into interstitial-intracellular space, and from there inside the cells [15, 18].

It is the free or unbound fraction of the drug that penetrates the membranes so that the equilibrium concentration in the interstitial fluid will be determined precisely by the unbound form of the drug. In general, the greater the level of drug binding to plasma proteins, the less the drug can leave the vessels, and the less will be its volume of distribution.

If medicinal substances have a high degree of binding to blood proteins, then their interaction is also probable at the distribution stage.

Albumins and acidic alpha-1 glycoprotein (AAG) are plasma proteins with which drugs are most often bound in plasma. Albumin can bind several endogenous and exogenous compounds, including fatty acids, metabolites, hormones, and many acidic (anionic) drugs. AAG can bind most drugs, mainly lipophilic bases (cations) and neutral ones [33, 34].

FDI at the distribution stage is explained, first of all, by the presence in food a biologically active substances that compete for binding sites with drugs (blood plasma proteins, receptors). For example, when food with a high caffeine content enters the body, caffeine is partially absorbed into the bloodstream and interacts with blood proteins. The introduced penicillins displace caffeine from its association with proteins, increasing the permeability of the blood-brain barrier for penicillins.

If food components bind to the same sites as drugs, the latter may be displaced from the binding site and have altered pharmacokinetic properties, such as fluctuations in distribution volume and bioavailability, which was observed with cyclosporine (in a well-dispersed chocolate emulsion). However, for most orally administered drugs, the clinical effects of altered plasma protein binding are minor [14].

Certain dietary restrictions and cachexia can decrease albumin and AAG concentrations, whereas a high-protein diet can increase them. Nutrients and their metabolites can also potentially affect the binding of drugs to plasma proteins. For example, increasing the concentration of fatty acids that strongly bind to albumin can allosterically modulate drug binding to albumin. Changes in blood glucose concentration, as observed in diabetes, also modulate albumin glycosylation and drug binding [15, 36].

Experimental studies found that albumin transports absorbed zinc to the liver, and also facilitates the absorption of Zn^{2+} by endothelial cells and erythrocytes. The conformation of the Zn^{2+}-binding site of albumin is affected by the presence of a fatty acid. Probably, fatty acids can modulate the affinity of albumin for Zn^{2+} [36].

Phenolic compounds such as flavonoids, phenolic acids, anthocyanidins, gallic acid derivatives, stilbene derivatives, etc. can form reversible complexes with plasma albumin. Flavonoids such as baicalin, rutin, and quercetin found in some dietary supplements have been suggested to alter albumin binding to drugs such as theophylline, nifedipine, promethazine, and ticagrelor. Regarding warfarin displacement, experimental results range from no risk to clinically significant FDIs. The fact is that S-warfarin (active enantiomer) has a lower connection with the protein [18, 37, 38].

After absorption, most drugs are transported from the gut via the portal vein to the liver before reaching systemic circulation. The intestinal epithelium also contains a rich network of lymphatic vessels. Lymph enters the systemic circulation directly, avoiding passage through the liver. Most drugs are not transported in significant quantities through the lymph. In contrast, food lipids and some highly lipophilic drugs, such as halofantrine, testosterone undecanoate, methylnortestosterone undecanoate and moxidectin can be transported by the lymphatic system, binding to lipoproteins, primarily chylomicrons (CMs) [39].

Food can affect the way of transport of highly lipophilic drugs from the intestines into the bloodstream, bypassing the portal vein, through the lymphatic system. Both the amount and type of dietary lipids affect the intestinal lymphatic transport of drugs, as some dietary lipids stimulate the formation of intestinal and thus increase the transport of lipids and lipophilic drug molecules such as halofantrine, cyclosporin A, amiodarone, amphotericin B, nystatin, eritoran, clozapine, haloperidol, paclitaxel. Long-chain lipids (olive, soybean oil, animal fats), but not short- or medium-chain lipids (coconut oil), are collected in the CMs and transported from the intestine by lymph. Also, mono- and polyunsaturated fats contribute more effectively to the formation of CMs and lymphatic transport of lipophilic substances than equivalent chain-length saturated lipids [15, 39].

However, the clinical significance of diet/food-induced changes in drug binding has not been demonstrated. Alteration of plasma protein binding is most

important for drugs with a high degree of binding (unbound fraction < 1%), which have a narrow therapeutic window [15].

1.1.1.3. Food influence on the drug metabolism and excretion

Recent preclinical and clinical studies have suggested that many food molecules can interact with metabolizing enzymes through different mechanisms. For example, the CYP3A, located in both the small intestine and liver, metabolizes various drugs including cyclosporine and terfenadine. Grapefruit juice has been reported to inhibit CYP3A isoenzymes and to increase the bioavailability of oral cyclosporine and terfenadine. Clinically significant interactions via CYP3A may also result from the consumption of food components that are inducers of CYP3A enzymes. For example, St. John's wort dietary supplements reduce the bioavailability of CYP3A substrates, which may necessitate dose adjustments of some drugs, such as cyclosporine and indinavir. Garlic has been shown to reduce the effects of saquinavir [15, 19].

Many foods have the ability to affect the P450 enzyme system. Vegetables and fruits can inhibit the activity of P450 enzymes: tomatoes inhibit CYP1A1, CYP1B1, red pepper - CYP1A2, CYP2A2, CYP3A1, CYP2C11, CYP2B1, CYP2B2, CYP2C6; grapefruit - isoenzymes CYP3A4, CYP1A2; mango – CYP1A1, CYP1A2, CYP3A1, CYP2C6, CYP2E1, apple – CYP1A1 isoenzyme. Food products can also act as enzyme inducers: broccoli and brussels sprouts activate the CYP1A2 enzyme; mandarin stimulates the activity of the CYP3A4 isoenzyme [40].

The final stage of the medicinal product in the body is excretion, which is primarily bile and kidney excretion. High-fat foods can stimulate bile secretion and therefore increase the bioavailability.

Low-sodium diets may result in decreased excretion and increased lithium toxicity, which is reabsorbed with sodium. For some acidic or basic drugs that depend on tubular reabsorption through a passive permeation mechanism, reabsorption and bioavailability may be altered if food intake alters urinary pH. For

example, a high-protein meal acidifies the urine, whereas a high-carbohydrate meal, a vegan diet or milk-rich consumption tends to make the urine more basic.

Weakly acidic drugs are more easily reabsorbed when the urine is acidic, while weak bases tend to be reabsorbed better when the urine is alkaline. Thus, manipulation of urine pH can be used to adjust the total systemic exposure of reabsorbed ionizing drugs [15].

1.1.2. Pharmacodynamic interactions

Pharmacodynamic FDI occurs due to specific pharmacological interactions between a drug and certain drinks or food. Some food products reduce or increase the effect and toxicity of drugs, affecting the drug PD.

Some vegetables (broccoli, brussels sprouts, kale, parsley, spinach, and others) have a high content of vitamin K that eating large quantities of these vegetables interferes with the safety and effectiveness of warfarin anticoagulant therapy [24].

ACE inhibitors can cause hyperkalemia, which can be dangerous. However, foods rich in [K^+], such as oranges and bananas, can cause hyperkalemia as well, which can lead to cardiac arrest and death due to arrhythmia. Cheese contains a substantial amount of tyramine. For this reason, persons taking MAOI antidepressants are cautioned to avoid foods that are rich in tyramine so that hypertensive crises can be avoided [41].

Conclusion for chapter 1

Literary data analysis on the mechanisms of food-drug interaction has been carried out. Food can significantly affect the pharmacological activity and safety of medicines. Thus, knowledge of the main aspects of the food-drug interaction, considering risk factors for dangerous interactions, as well as a well-established

system for informing the population about clinically significant interactions, can improve the effectiveness and safety of pharmacotherapy.

CHAPTER 2
MATERIALS AND METHODS OF RESEARCH

2.1. The design of a questionnaire to assess pharmacy students' awareness of food-drug interactions

To collect data from respondents, we used a structured questionnaire consisting of standardized closed questions and predefined answers. This allows to significantly speed up the process of processing questionnaires, although the development of such questionnaires takes more time. The collected data is as objective as possible, but the information may be incomplete. When creating the questionnaire, we considered general design concepts, including item creation and analysis, interpretability of terms, assessment of validity and reliability, and specific patient-initiated questions asked during a consultation.

In the study, pharmacy students' awareness of FDI issues was assessed using a questionnaire developed by us. First, the questionnaire was tested in a pilot study on a convenience sample of 10 student pharmacists to ensure the reliability and comprehensibility of the content of the questionnaire.

Our research was conducted in February-March 2023. The object of the study was pharmacy students of the National University of Pharmacy. Respondents were selected as a random sample.

The questionnaire developed by us includes the following parts: an explanatory part, which provides information about the tasks and content of the questionnaire, instructions for respondents, and an evaluation part. The evaluation part consists of 31 questions and includes three sections: I – questions on socio-demographic characteristics (age, gender, place of residence, course of study), II – 9 general questions related to the understanding of pharmacy students of the FDI problem, III – 18 closed questions to assess respondents' knowledge of common FDIs. This section includes FDIs that have been cited in previous studies, some of which may affect serious side effects (grapefruit with atorvastatin, MAOIs with

cheese, spironolactone with moderate potassium intake, warfarin with vitamin K supplements, theophylline with excessive amounts of coffee and/or tea), others can significantly decrease the effectiveness of drugs, especially if a specific food is consumed regularly in large quantities or with drugs with a narrow therapeutic index (tetracycline with milk and dairy products, levodopa with protein food). The third section included questions about the effect of consumed beverages on medication and 5 questions to assess knowledge of the appropriate timing of medication intake in relation to food.

Questionnaire

I. General information

1. Please indicate the course of your studies at NUPh
   - 3 course
   - 4 course
   - 5 course
2. Please indicate your age
   - ≤ 21 years
   - 22
   - 23
   - 24
   - 25
   - 26
   - 27
   - More than 27
3. Please indicate your gender.
   - female
   - male
4. Please indicate the country of your permanent residence

_____ (open-ended question)

II. Special part

5. What do you think: can food-drug interaction increase the effect of the drug?

– Yes
– No
– Difficult to answer

6. What do you think: can food-drug interaction decrease the effect of the drug?

– Yes
– No
– Difficult to answer

7. What do you think: can food-drug interaction lead to serious side effects?

– Yes
– No
– Difficult to answer

8. Do you think it is important to consider food-drug interactions?

– Yes
– No
– Difficult to answer

9. Do you think you have enough information about food-drug interactions?

– Yes
– No
– Difficult to answer

10. Would you like to know more about food-drug interactions?

– Yes
– No
– I don't know it's hard to decide

11. What are your main sources of information about food-drug interactions? (multiple answers can be selected)

- Knowledge acquired at the university
- Instructions on the medicine or Medication Guides
- Drug promotional materials
- Information from medical representatives of drug manufacturing companies
- Science articles
- Mass media

12. Can a patient-related factors such as age impact on the risk of food-drug interaction?

- Yes
- No
- Difficult to answer

13. Can a patient-related factor such as the health status impact on the risk of food-drug interaction?

- Yes
- No
- Difficult to answer

14. Do drugs with a narrow therapeutic index have a high risk of food-drug interaction?

- Yes
- No
- Difficult to answer

15. What advice would you give to a patient who wants to get the information about food-drug interactions?

- To visit a doctor
- To ask the pharmacist at the pharmacy
- To find information in the instructions on the medicine

- To find information in a medication guide
- To find information on the internet

16. Is it save to take nifedipine with grapefruit juice?

- Yes
- No
- Difficult to answer

17. As a result of the interaction of nifedipine with grapefruit juice, the effect of nifedipine will

- Increase
- Decrease
- Not change
- Difficult to answer

18. Should patients be advised to eat a lot more vitamin K-rich food during warfarin treatment?

- Yes
- No
- Difficult to answer

19. Should patients limit their intake of caffeine-containing beverages during theophylline treatment?

- Yes
- No
- Difficult to answer

20. Does milk influence the effectiveness of tetracycline?

- Yes
- No
- Difficult to answer

21. How can tetracycline adsorption change by administration with milk?

- Decrease
- Increase

– Difficult to answer

22. Should patients taking monoamine oxidase inhibitors (MAOI) avoid cheese consuming?

– Yes
– No
– Difficult to answer

23. Should patients limit their intake of potassium-rich foods while taking spironolactone?

– Yes
– No
– Difficult to answer

24. Should patients limit their intake of potassium-rich foods while taking enalapril (ACE inhibitor)?

– Yes
– No
– Difficult to answer

25. Should patients limit your protein intake while taking levodopa?

– Yes
– No
– Difficult to answer

26. Which drink is often taken medicines with?

– Tea
– Coffee
– Drinking water
– Distilled water
– Milk
– «Fanta», «Coca-cola»
– Fruit juices

27. When to take omeprazole?

- Before eating or with food
- After eating
- On an empty stomach
- Not dependent on food
- Difficult to answer

28. When to take acetylsalicylic acid uncoated tablets?
    - Before eating
    - With food
    - After eating
    - On an empty stomach
    - Not dependent on food
    - Difficult to answer
29. When to take Aspirin Cardio Enteric-Coated Tablets?
    - No earlier than 30 minutes before a meal
    - With food
    - Immediately after eating
    - Not dependent on food
    - Difficult to answer
30. When to take the hypoglycemic drug metformin?
    - Before eating
    - With food or after eating
    - On an empty stomach
    - Not dependent on food
    - Difficult to answer
31. When to take the antibiotic azithromycin?
    - Before eating
    - With food
    - 1 hour before or 2 hours after a meal
    - Not dependent on food
    - Difficult to answer

2.2. Statistical analysis

The data obtained as a result of the survey were statistically processed using the Excel program, the package of statistical programs STATISTICA 10.0 (StatSoft). Comparative intergroup analysis was performed using Fisher's test φ (if necessary, with Yates correction) and the relationship between individual indicators was based on Spearman's correlation coefficient ρ. A value of $p < 0.05$ was considered statistically significant.

Conclusions for chapter 2

Thus, at the initial stage of the research, a questionnaire was developed to assess the awareness of pharmacist students about the FDI. The accessibility (comprehensibility) and resolution of the questionnaire questions were checked on a small sample of respondents. The minimum sample volume was calculated and methods were chosen for further statistical analysis of the results.

CHAPTER 3
EVALUATION OF PHARMACY STUDENTS' AWARENESS OF FOOD-DRUG INTERACTIONS

3.1. Characteristics of survey respondents

To evaluate the pharmacy students' awareness of FDI, as well as the respondents' attitude to this issue, we collected empirical information in a questionnaire survey. The structured questionnaire was conducted during February-March 2023 among pharmacy students of 3, 4 and 5 years of study in NUPh.

In total, 102 people took part in the survey, of which 3rd year students – 19 (18.6%), 4th year students - 15 (14.7%), 5th year students - 68 (66.7%). The survey results are shown in figure 3.1.

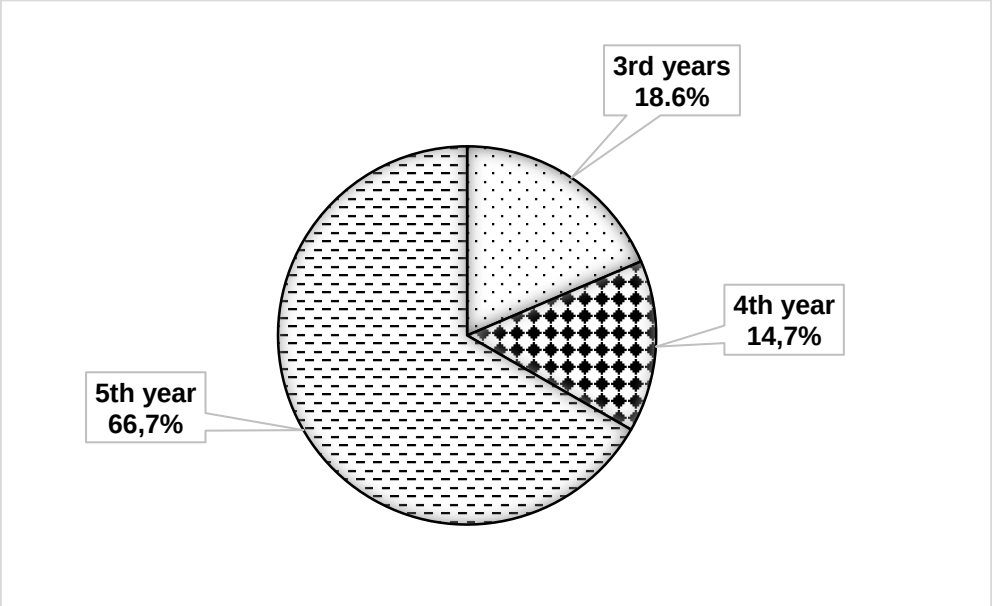


Fig. 3.1. Distribution of the respondents according to year of study

The age categories of respondents were: < 21 years (15.6%), 22 years (8.8%), 23 years (20.6%), 24 years (19.6%), 25 years (8.8%), 26 years (2.0%), 27 years (11.8%), >27 years (12.7%). The survey results are shown in Figure 3.2.

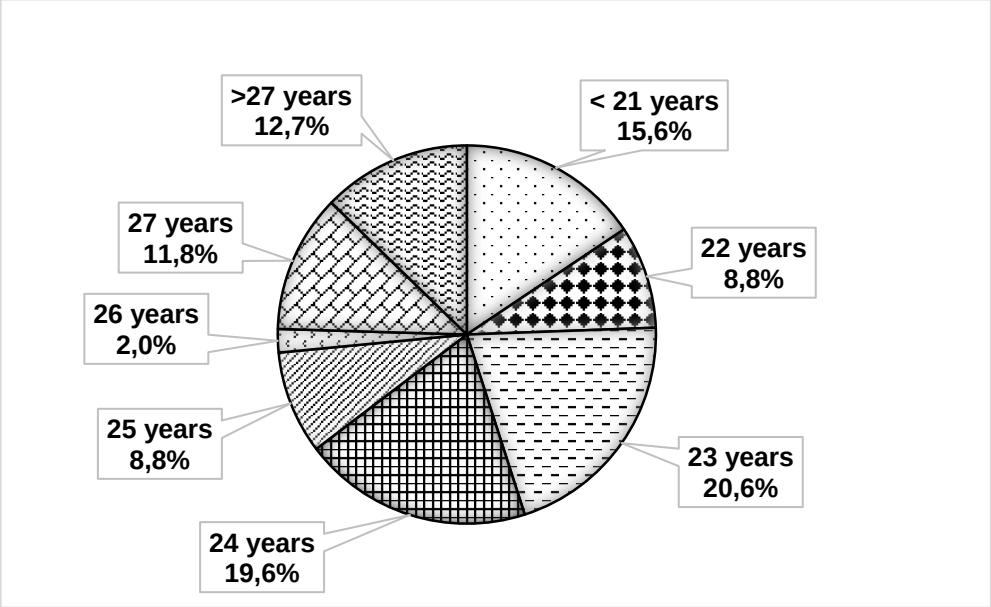


Fig. 3.2. Distribution of the respondents according to their age

The phenomenon of professional horizontal segregation, characterized by a clear division of economic sectors between genders, is widely represented in the world. Until the beginning of the 20th century, pharmacy was the men's monopoly [42]. Today, the distribution of many sectors of the economy between genders has changed. Pharmacy is no exception. Thus, among our respondents, women accounted for 49% (50 people), and men – 51% (52 people). The survey results are shown in Figure 3.3.

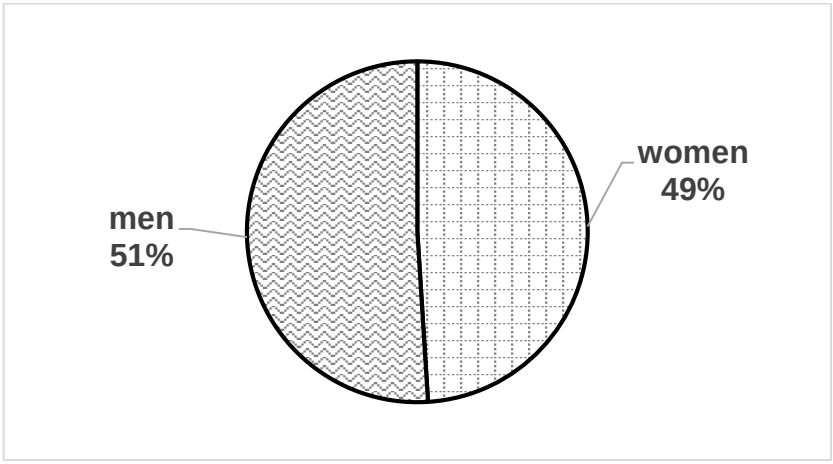


Fig. 3.3. Distribution of the respondents according to gender

64 (62.7%) students named Morocco as their place of permanent residence, 21 (20.6%) students - Ukraine, 4 (3.9%) students - Germany, 3 students (2.9%) - Lebanon, 1 student each (1.0%) - Kuwait, Portugal, Spain, Turkey, 4 (3.9%) students did not want to specify.

An increasingly important problem in pharmacy is the practical application of knowledge gained in the learning process, on the one hand, and the impact of practical work experience on the acquisition and consolidation of skills and knowledge, on the other hand.

Among the respondents, all 5-year students already had experience working in a pharmacy, possibly in the form of an internship, wich is provided by the training program at NUPh. That is, the majority of respondents had little work experience in their specialty.

3.2. Assessment of the food-drug interaction problem from the point of view of pharmacy students

The introduction of any drug into the body is associated with a potential risk of adverse reactions. There are a number of non-modifiable (for example, age and female gender) and modifiable factors that increase the risk of their development. One of the modifiable risk factors for drug-induced diseases is the FDI, in addition, such an interaction can reduce the effectiveness of pharmacotherapy [4, 5]. Joint Commission on Accreditation of Healthcare Organizations (JCAHO) standards state that patients must be provided with instructions on potential drug/food interactions. The major goals of a drug/food interaction program are to inform the patient of potential interactions and to educate them on how to adjust their food intake to prevent them [43].

It is important that health professionals, such as physicians, pharmacists and dieticians, are familiar with FDI issues and promote effective pharmacotherapy. Minimizing adverse FDI will improve patient care by optimizing therapeutic effects and maintaining adequate nutritional status.

It was interesting to learn how pharmacy students approach the problem of FDI.

Almost all students (100 – 98,0%) pay great attention to FDI and think that it should be taken into account when treating patients. The majority of respondents consider that FDI can increase the effect of the drug – 91 (89.2%); to reduce the effect of the drug – 92 (90.2%), lead to serious adverse reactions – 92 (90.2%). The results are shown in table 3.1.

Table 3.1.

Attitude of pharmacy students to the issue of FDI;

Questions	Numbers of answers (%)		
	Yes	No	Difficult to answer
What do you think: can FDIs increase the effect of the drug?	91 (89.2%)	10 (9.8%)	1 (1.0%)
What do you think: can FDIs decrease the effect of the drug?	92 (90.2%)	10 (9.8%)	-
What do you think: can FDIs lead to serious side effects?	92 (90.2%)	10 (9.8%)	-
Do you think it is important to consider FDIs?	100 (98.0%)	2 (0.2%)	-

A little less than half of pharmacy students 44 (43.1%) consider that they lack information about FDI. Almost half of respondents 50 (49.0%) think that they have enough information about FDI. The results are shown in Fig. 3.4.

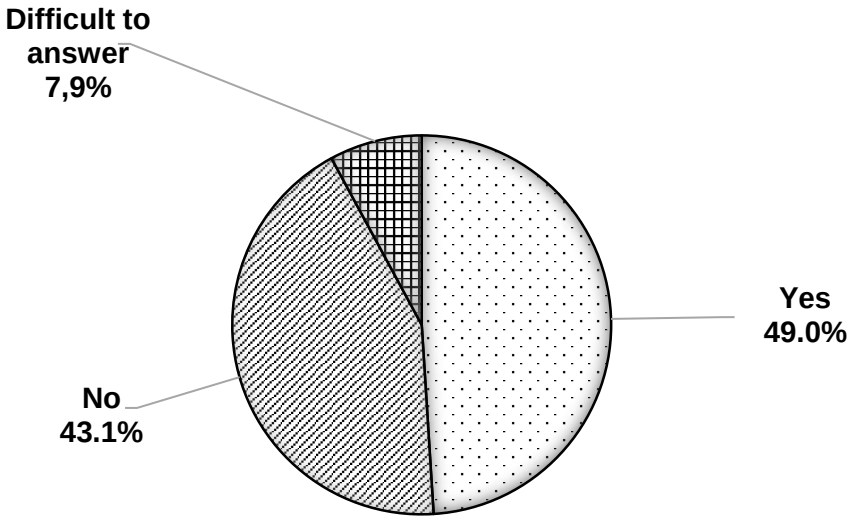


Fig. 3.4. Answers of pharmacy students to the question "Do you think you have enough information about FDIs?"

The vast majority of students (95 – 93.1%) would like to know more about food-drug interactions, 6 (5.9%) respondents were undecided, and only 1 student answered no. The results are shown in Fig. 3.5.

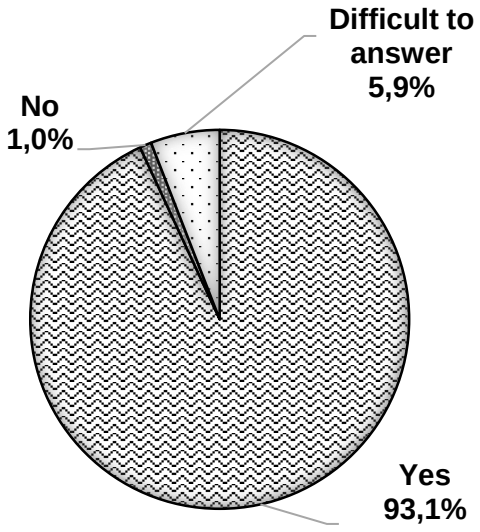
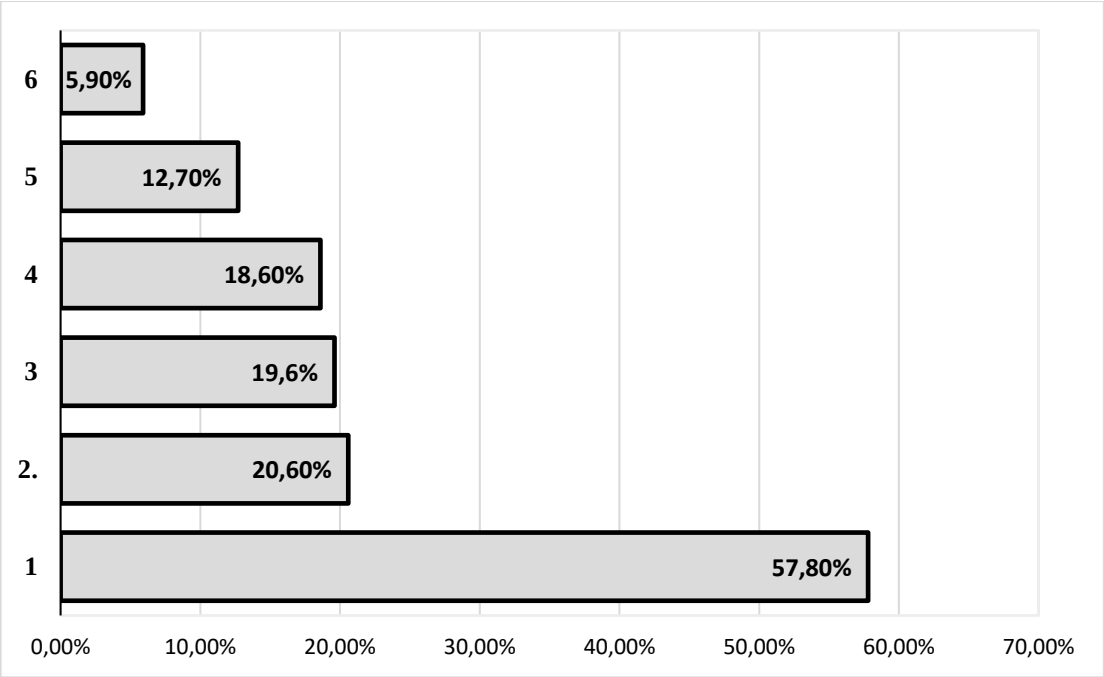


Fig. 3.5. Answers of pharmacy students to the question "Would you like to know more about FDIs?"

Data analysis revealed the educational needs of pharmacy students. Meeting various learning needs will foster pharmacists in their current and future professional roles. These findings will be of interest to employers and educators in supporting pharmacists' evolving roles in practice.

The pharmacy students were asked to choose the main sources of their knowledge about FDI (several sources). As the main information sources 59 (57,8%) respondents chose the knowledge acquired at the university, 21 (20,6%) – information from medical representatives of drug manufacturing companies, 20 (19,6%) – instructions on the medicine or medication guides, 19 (18,6%) – mass media, 13 (12,7%) – science articles, 6 (5,9%) – drug promotional materials. The survey data are shown in Fig. 3.6.



1 - Knowledge acquired at the university
2 - Information from medical representatives of drug manufacturing companies
3 - Instructions on the medicine or Medication Guides
4 - Mass media
5 - Science articles
6 - Drug promotional materials

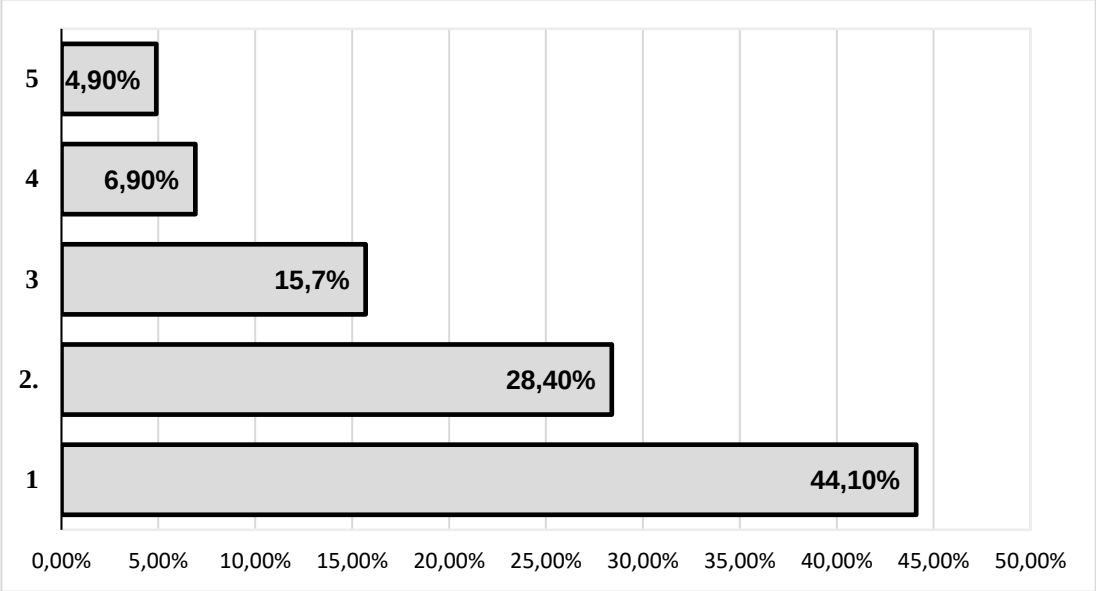
Fig. 3.6. The main information sources about FDI for respondents

The impact of food and drug interactions depends on a variety of intervening factors like: dosage of the drug, person's age, sex, size or weight of the person, state of health, nutritional status and time of the drug taken. Dangerous consequences will be for drugs with a narrow therapeutic index. The risks of FDI grow with the increase in the dose and duration of taking the drug [15, 44, 45].

Abdollahi M. et al. found that age, polypharmacy, and disease duration were statistically significantly associated with a higher risk of potential food-drug interactions (the longer it lasts, the higher the risks). Similar data were obtained by Neves SJF et al., who concluded that polypharmacy, simultaneous intake of drugs and food, lack of counseling on the correct drug intake, as well as the presence of certain chronic diseases (diabetes mellitus) increase the risk of adverse reactions due to FDI [46, 47].

66 (64.7%) respondents consider that such exogenous factors as the narrow therapeutic index of drugs affect the FDI, and pharmacists answered that endogenous factors such as the age 78 (76.5%) and health status of patients 90 (88.2%) are important in the case of FDI.

To obtain information on the combined intake of food and medicines, pharmacy students, first of all, would recommend pharmacy visitors to seek advice from a doctor (45 – 44.1%) or pharmacist 29 (28.4%), carefully read the instruction for the use of medicine - 16 (15.7%). A smaller number of respondents consider it appropriate to look for information in special medication guides (7 – 6,9%) or on the Internet (5 - 4.9%). The results of the survey are shown in Fig. 3.7.



1 – To visit a doctor
2 – To ask the pharmacist at the pharmacy
3 – To find information in the instructions on the medicine
4 – To find information in a medication guide
5 – To find information on the Internet

Fig. 3.7. Respondents' answers to questions «What advice would you give to a patient who wants to get the information about food-drug interactions?»

3.3. Assessment of respondents' awareness of drug-food interactions

Pharmacists through their knowledge base in health care can play an influential informative role. To provide advice to pharmacy visitors, a pharmacist must be familiar with the issues of FDI, so we were interested in how well the surveyed students knew about this issue.

It has been reported that grapefruit juice causes a pharmacokinetic interaction with many drugs after co-ingestion. It is postulated that the substances in grapefruit juice may inhibit the first-pass metabolism during the intestinal absorption process. In recent years, several furanocoumarin derivatives (such as bergamottin and 6′,7′-dihydroxy-bergamottin) that inhibit P450 CYP3A enzymes in intestinal microsomes were isolated from grapefruit juice. A significant effect of grapefruit juice on the absorption of drugs metabolized by CYP3A4 has been demonstrated in humans.

This interaction was discovered accidentally during the study of the interaction of felodipine (dihydropyridine, a Ca^{2+} antagonist) and ethanol. Grapefruit juice was used to mask the taste of ethanol. Felodipine underwent high presystemic (first pass) metabolism mediated by CYP3A4 in the intestine and liver, resulting in a 15% decrease in bioavailability. Further studies showed that grapefruit juice reduced the presystemic metabolism of felodipine through interaction with the intestinal wall CYP3A4. Thus, the effect of grapefruit juice may lead to an increase in the concentration of felodipine in the systemic circulation (systemic AUC and C_{max}), and this effect may last longer than 24 hours.

250 ml of grapefruit juice increases AUC and C_{max} to 267% and 345%, respectively. The combined intake of grapefruit juice and felodipine led to a decrease in blood pressure and, more often, orthostatic hypotension.

In most cases, the interaction is limited to oral (rather than intravenous) drug administration, indicating the importance of intestinal CYP3A in mediating food-drug interactions [15].

We asked the respondents to answer the question regarding the consultation of the pharmacy visitor on the issue of simultaneous intake of felodipine together with grapefruit. The correct answer was given by 83 (81.4%) respondents, they consider that it is impossible to take them simultaneously. 14 (13.7%) answered that they can be taken simultaneously and 5 (4.9%) respondents found it difficult to answer this question. 54 (52.4%) of the respondents know that the result of the interaction of felodipine and grapefruit is an increase in the effect of drug. And such interaction is dangerous. During the entire period of treatment with felodipine, the patient should be advised to completely refrain from eating grapefruit or its processing products. The results of the answers are given in table 3.2.

Table 3.2.

Distribution of respondents' answers to the questions about FDI

FDI	Correct answers	Incorrect answers	Difficult to answer
Is it save to take nifedipine with grapefruit juice?	83 (81.4%)	14 (13.7%)	5 (4.9%)
As a result of the interaction of nifedipine with grapefruit juice?	54 (52.4%)	34 (33.3%)	14 (13.7%)
Should patients be advised to eat a lot more vitamin K-rich food during warfarin treatment	57 (55.9%)	27 (26.5%)	18 (17.6%)
Should patients limit their intake of caffeine-containing beverages during theophylline treatment	66 (64.7%)	28 (27.5%)	8 (7,8%)
Does milk influence the effectiveness of tetracycline?	89 (87.3%)	7 (6.9%)	6 (5,9%)
How can tetracycline adsorption change by administration with milk?	73 (71.6%)	18 (17.6%)	11 (10.8 %)
Should patients taking monoamine oxidase inhibitors (MAOI) avoid cheese consuming	71 (69.6%)	13 (12.7%)	18 (17,6%)
Should patients limit their intake of potassium-rich foods while taking spironolactone?	72 (70.6%)	17 (16.7%)	13 (12.7%)
Should patients limit their intake of potassium-rich foods while taking enalapril (ACE inhibitor)?	61 (59.8%)	27 (26.5%)	14 (13.7%)
Should patients limit your protein intake while taking levodopa?	53 (52.0%)	29 (28.4%)	20 (19.6%)

Vitamin K is a nutrient essential for heart and bone health. It is important to consider the role of vitamin K in warfarin treatment. The mechanism of action of the drug consists in blocking the action of vitamin K by inhibiting the enzyme epoxide reductase, and, as a result, inhibiting the synthesis of blood coagulation factors II, VII, IX and X, as well as two anticoagulant proteins (proteins C and S). Foods rich in vitamin K are green vegetables such as lettuce, spinach and broccoli. If you are taking warfarin, it is important to have a consistent amount of vitamin K in your diet. If your diet is low in vitamin K, a sudden burst of the vitamin can increase your risk of bleeding. Dietary counseling should be given to the patient to obtain an adequate and constant supply of vitamin K. The most important advice for patients taking warfarin is to stick to their usual diet and to report any planned changes in diet or multivitamin use [48, 49].

Certainly, patients should not be advised to eat more vitamin K-rich leafy green vegetables during warfarin treatment. 57 (55,9%) respondents have given the correct answer to this question, 27 (26,5%) have given the wrong answer, and it was difficult to answer for 18 (17,6%) respondents (see table 3.2).

Common foods and beverages that contain caffeine, including coffee, tea, cola, and chocolate, can interact with theophylline. Side effects of theophylline, such as nausea, irritability, nervousness, rapid heartbeat, tremors, or sleep disturbances, may get worse if you consume too much caffeine. Caffeine consumption should be limited while taking theophylline. Many over-the-counter medications and dietary supplements may also contain caffeine.

In our survey 66 (64,7%) respondents consider that it is necessary to avoid excessive consumption of caffeine-containing beverages in patients taking theophylline, 28 (27,5%) respondents do not consider it appropriate, it was difficult to answer 8 (7,8%) to pharmaceuticals (see table 3.2).

Food can remove active ingredients of medicine through the chelation process. Certain food contains divalent metal cations such as Ca^{2+}, Mg^{2+} and Fe^{2+} can chelate with some drug molecules (for example, bisphosphonates, tetracyclines, ciprofloxacin). These complexes are unavailable for absorption. Tetracyclines

should be taken separately from milk or dairy products, which contain these minerals. Recent studies in healthy volunteers have shown that even a relatively small volume of milk containing extremely low amounts of calcium can seriously impair the absorption of this drug [15].

In our survey, 89 (87,3%) pharmacy students know that milk decreases the effectiveness of tetracycline treatment, 7 (6,9%) respondents think that - "no", for 12 (11.5%) - it was difficult to answer (see table 3.2).

Cheese, smoked meats, alcoholic beverages, fava beans, and fermented food contain high levels of tyramine that promote blood pressure elevation or even a hypertensive crisis when ingested concurrently with MAOIs. This is a result of a decrease in tyramine degradation that leads to stimulates the release of endogenous catecholamines (adrenaline, norepinephrine), the breakdown of which is also inhibited due to the inhibition of MAO [50].

Therefore, do not forget to warn the pharmacy visitor taking MAO inhibitors about the need to follow a diet, the violation of which can lead to a fatal outcome. The fact is that cheese syndrome develops very quickly – 15-90 minutes after consuming a potentially dangerous product during MAOI treatment.

In this study, the question about food interaction with MAOIs was answered correctly by 71 (69.6%) respondents, 13 (12.7%) students think that patients taking MAOIs should not avoid cheese consumption, for 18 (17.6%) respondents it was difficult for the respondents to answer this question (see table 3.2.).

Under the influence of spironolactone and enalapril, due to a decrease in aldosterone secretion, the excretion of K^+-ions with urine decreases. Therefore, together with these drugs, the use of dietary supplements or salt substitutes containing potassium should be limited to prevent the risk of hyperkalemia.

Patients taking spironolactone and enalapril should limit the use of potassium-containing food products. In this study, 72 (70.6%) and 61 (59.8%) respondents knew about the interaction between potassium with spironolactone and potassium with enalapril respectively (see table 3.2.).

On a similar note, levodopa competes with amino acids for absorption, hence co-administration of the drug with protein-rich food would result in reduced effectiveness.

It has been shown that a patient condition with Parkinson's disease was better on a low protein diet compared to a high protein diet. Theoretically, this can be explained by the competitive absorption of oligopeptides and levodopa using oligopeptide transporters (PEPT1) in the apical membranes of intestinal epithelial cells [15].

Therefore, patients taking levodopa should avoid a high-protein diet. And more than half of pharmacy students (53 – 52.0%) who participated in this study recognized that protein rich food affects the efficacy of levodopa (see table 3.2.).

Water is considered the best beverage to take your medicines with. The water should ideally be at room temperature. Fresh drinking water does not inhibit drug metabolism nor does it interfere with its quick absorption in the body. Capsules must always be taken with water at room temperature. Hot water causes the capsule coating to dissolve in the mouth or at the initial stage. However, paracetamol should be taken with hot water, as paracetamol dissolves faster in hot water and can therefore be absorbed more quickly.

Other beverages like soft drinks or aerated beverages, coffee or tea, milk and alcohol can often cause some drug interactions or allergies in the case of few patients. While milk is safe to be consumed with calcium or vitamin D tablets, it may not be as safe with all other medications.

Purported health benefits of certain plant products have led to their use by patients as complements (or alternatives) to drug therapy. The popular consumption of fruit juices, green teas, plant teas, the vine is attributed not only to taste and nutritive value but also to increase awareness of the pharmacologic (e.g., antioxidant) effects of specific constituents. However, in parallel, a growing number of in *vitro* and in *vivo* studies have demonstrated their inhibitory, potentially detrimental, effects on enzymes and transporters involved in drug disposition [18].

Among all liquids, milk interacts most actively with medicine. Dairy products such as milk, yogurt, and cheese can reduce drug absorption and, as a result, bioavailability and effectiveness.

Absorption of tetracycline antibiotics decreases by 20-80% when taken with milk. Penicillins, cephalosporins, fluoroquinolones, lincomycin, ketoconazole, and clotrimazole should not be taken with milk for the same reason. Milk and dairy products also interfere with the absorption and action of iron preparations and caffeine. In case of an overdose, milk can be used as an antidote. Due to the slightly alkaline pH, milk cannot be combined with acidic medicinal substances: derivatives of salicylic acid, barbiturates, as well as antacids. It is not recommended to drink pancreatin preparations and any preparations in an acid-resistant shell with milk.

However, some drugs are recommended to be taken with milk. For example, nonsteroidal anti-inflammatory drugs (butadione, indomethacin, diclofenac, etc.), while milk forms a protective film on the mucous membrane of the gastrointestinal tract and thus reduces the irritating effect of the drug. In order to protect the mucous membrane, it is also advisable to take papaverine hydrochloride, dipyridamole and potassium iodide with milk.

Vitamin D and other fat-soluble vitamins (A, E, K) are absorbed better if taken with milk. However, this increases the risk of overdose [5,15].

It is very important to pay attention to the simultaneous use of drugs and alcohol. The consumption of alcoholic beverages can alter or pervert the effects of drugs and increase toxicity. The concurrent intake of such drugs as neuroleptics, analgesics, antidepressants, diuretics, anti-inflammatory drugs, insulin, nitroglycerin and antibiotics together with alcohol can lead to severe poisoning, often fatal. For example, long-term combined use of non-steroidal anti-inflammatory drugs and alcoholic beverages can cause damage to the gastric mucosa and the formation of ulcers. Ethanol potentiates the hepatotoxic effect of paracetamol, metronidazole [15, 51, 52].

Several juices were found to have an interaction with medication by metabolizing and altering transporters enzymes to a wider degree than initially described.

Grapefruit juice is one of the most dangerous beverages in combination with drugs. It inhibits intestinal and liver cytochromes, thus slowing down the metabolism of more than 70% of medicines, as a result, overdose phenomena with corresponding undesirable effects may be observed. For example, it is not recommended to use HMG-CoA reductase inhibitors (statins) with grapefruit juice, because this increases the level of statins in the blood, thereby increasing the risk of adverse reactions; the bioavailability of calcium channel blockers is also increased. An increasing number of adverse drug reactions might be avoided based on knowledge about the interaction of grapefruit juice and relevant drugs. Therefore, patients need to be educated about the hazards of grapefruit juice interaction with medication [5,15, 53].

Cranberry juice also increases the bioavailability of CYP3A4 isoenzyme substrates - calcium antagonists. Naringin, an ingredient in most citrus fruits has been shown to reduce aliskiren uptake. Apple juice can also affect drug metabolites *in vitro* and human volunteers. There is evidence that apple juice inhibits the activity of OATPs, which facilitate the absorption of several endogenous compounds such as hormones and bile acids. In a randomized crossover study involving 14 healthy volunteers, it was found that apple juice decreased the bioavailability of fexofenadine compared to water. Citrus fruits should be avoided when combined with corticosteroids, macrolides, sedatives and antiepileptic drugs. Pomegranate juice should not be washed down with antiepileptic drugs [24, 50, 54].

During our survey, pharmacy students answered that as a rule it is better to take medicines with drinking water (86 – 84.3%), distilled water (8 – 7.8%), juices (4 – 3.9%), tea (3 – 2.9%), milk (1 – 1.0%). Water remains the best beverage to take medicines with, if it is not indicated instructions.

Administration of drugs before, with, and after food intake can affect the absorption, distribution, metabolism, and excretion of the drugs. The time of administration of medication should be considered during patient counseling. It is a

typical question by patients especially when the medicine is prescribed for the first time. Pharmacists have to exploit their knowledge to maximize therapeutic effectiveness whilst also minimizing or avoiding adverse effects. The conditions for taking the drug (before or after food, chewing or not, what to drink, what to dilute, etc.) are specified in most instructions, in “the dosage and administration” section. Medicine should be taken on an empty stomach (one hour before eating or 2 hours after) unless advised otherwise.

An example of the food effect on the pharmacokinetic profile of drugs is the change in the bioavailability of the tyrosine kinase inhibitor lapatinib: the bioavailability of lapatinib at a single dose of 1,500 mg after taking it together with a high-calorie standard diet increases by an average of 325% - 4.25 times, compared with fasting. In other words, the blood serum concentration of the drug after taking one tablet at the same time with food is comparable to taking 4 tablets on an empty stomach [55].

A study by Abdollahi M et al., based on medical data from 400 hospitalized patients, examined the risks of potential interactions between food and 19 commonly prescribed medications. As the analysis showed, drugs were often prescribed without considering the time of food intake, and therefore had high risks of interactions and, as a result, changes in efficacy and safety profiles, for example, due to changes in the blood plasma concentration of drugs.

Omeprazole reduces the amount of acid production in the stomach. It belongs to a group of proton pump inhibitors. These medicines are most effective if taken immediately after or during a meal. Omeprazole capsules are usually taken once a day, preferably in the morning, right before a meal or on an empty stomach 20 minutes before a meal with a small amount of water. Omeprazole capsules should be swallowed whole. Some medicines (aspirin and other non-steroidal anti-inflammatory drugs) can irritate the stomach mucous membrane, and taking them after food will reduce this side effect. But enteric-coated tablet "Aspirin Cardio" is recommended to be taken at least 30 minutes before meals to avoid the release of the active substance before reaching the alkaline medium of the intestine, tablets

should not be crushed, broken or chewed because this will damage the enteric coating. Oral antidiabetic medicines like metformin usually be taken around meal times.

So, taking medicines at the right time is very important. In our study, the vast majority of pharmacy students correctly indicated how to take the medication concerning food: for azithromycin – 71 (69,6%) and acetylsalicylic acid 68 (67,7%). The worst knowledge about the timing of drug intake was for metformin, "aspirin cardio" and omeprazole. The survey results are shown in Table 3.3.

Table 3.3.

Distribution of respondents' answers about timing of drug intake with relation to food

Drug name	Correct answers	Incorrect answers	Difficult to answer
Omeprazole	48 (47,1%)	47 (46,1%)	7 (6,8%)
Acetylsalicylic acid	68 (66,7%)	29 (28,4%)	5 (4,9%)
Aspirin cardio	50 (49,0%)	41 (40,2%)	11 (10,8%)
Metformin	63 (61,8%)	27 (26,5%)	12 (11,8%)
Azithromycin	71 (69,6%)	27 (26,5%)	4 (3,9%)

In addition, the timing of meals and medications plays an important role. Understanding the possible clinical implications of taking medicines with or without a meal is important for achieving quality use of medicines. Although the effect of food is not clinically important for many drugs, there is FDI that may have adverse consequences. Often these interactions can be avoided by advising the patient how to take the medication concerning food intake. To avoid FDI, it is not often necessary to stop taking drugs or eating certain foods. For example, to prevent the interaction of tetracycline and dairy products, they should be taken at different times.

As our questionnaire showed, student pharmacists need to improve their knowledge of FDI to provide professional consultations to patients. Our results are

consistent with previous studies that reported a lack of awareness among pharmacists and other health care professionals about FDI [50].

3.4. Pharmaceutical care: food-drugs interaction

Giving patients information about drugs, pharmacists often discuss possible side effects and how to take drugs. Pharmaceutical care also includes recommendations and consultations for the patient on the interaction of the drug food, alcohol; optimal time of day to take.

The pharmacist, together with the prescriber, is obliged to make sure that the patients are aware of the risk of side effects and have an appropriate algorithm of action in case of their occurrence. Pharmacists possessing medical knowledge, can relate unexpected symptoms that occur in a patient to possible adverse consequences of their drug therapy. Sufficient information about medications and when to take them with food can help avoid problems with drug interactions.

- When dispensing medications to patients, the pharmacist may provide the following information:
  - Read the recommendations for taking the medicine in the prescription. If you do not understand something or think you need more information, ask your doctor or pharmacist.
  - Read the instructions for the use of the drug you are taking or intend to take, paying attention to which food should be removed from your diet during treatment with;
- Even over-the-counter medications can cause problems. As a general rule, it is best to take most medications with water.
- Do not add medicine to food (unless directed by a doctor). This may affect the effectiveness of the medication.
- Do not take vitamin preparations or dietary supplements without consulting a doctor during treatment with drugs. Vitamins and minerals can interact with some medications.

- Do not mix the medicine with hot drinks, as this may affect the effectiveness of the medicine. Alcohol should always be avoided when taking any medication. Alcohol can decrease the absorption of the medication, dissolve the coating of some tablets and capsules, interact directly with medications, and increase drowsiness.
- Tell your doctor and pharmacist about prescription or over-the-counter medicines, and dietary supplements you are taking.
- Check with your pharmacist or doctor about how food might affect the medicines you are currently taking.
- You should avoid taking drugs with caffeine containing beverages (tea, coffee, Coca-Cola, etc.), carbonated drinks and milk. Some medicines can irritate the gastrointestinal mucosa, and taking them with milk will reduce this effect.
- Pay attention to the consumption of fruit juices, especially citrus fruits. Their use during pharmacotherapy in many cases leads to an increase in the blood level of drugs, such as statins, antibiotics, sedatives, antiarrhythmic drugs, etc., which increases the risk of adverse reactions;
- Some drugs need to be taken at certain times with meals. Talk to your doctor or pharmacist about the correct way and time to take your medicine.
- Contact your doctor if your health problems do not disappear with treatment or if your health condition worsens.
- During pregnancy and lactation, always consult your doctor or pharmacist before taking any medicine.

Conclusions for chapter 3

1. A total of 102 pharmacy students studying at the Pharmaceutical faculty and the Faculty for foreign citizens' education of the National University of Pharmacy in the 3rd, 4th and 5th year, took part in our survey.
2. As the survey has shown, the vast majority of pharmacy students think that food can affect the effectiveness and safety of pharmacotherapy, and 98.0% of students claim that it is important to consider FDIs.
3. About half (49%) of the interviewees claimed that they have enough information about FDI. Knowledge acquired at the university, information from medical representatives of drug manufacturing companies, instructions on the medicine or medication guides were noted as the main sources of information on this issue for them. 98.0% of students claim that it is important to consider FDIs. The vast majority of students (93 %) would like to know more about food-drug interactions.
4. Regarding questions about FDIs, pharmacists demonstrated better knowledge, mainly regarding the interactions of tetracycline with milk, felodipine with grapefruit, MAOI with cheese, spironolactone with potassium-rich food, the timing of administration about food for azithromycin and aspirin. This can be explained by the fact that these cases are well-known examples in literature and special education. But fewer respondents gave correct answers to other questions.
5. The obtained results indicate the inadequacy of pharmacy students' knowledge on a number of issues of the research topic and set the goal of further consideration of the research results when revising educational and professional programs and improving the content of educational components.
6. The results can be used by education and healthcare professionals to develop appropriate educational interventions to promote knowledge of clinically relevant FDIs among pharmacists and other healthcare professionals.

CONCLUSIONS

1. Literary data analysis on the mechanisms of food-drug interaction has been carried out. Food can significantly affect the pharmacological activity and safety of medicines. Therefore, we set a goal to investigate the attitude and pharmacy student's awareness regarding the issues of FDI.
2. We developed a questionnaire to assess the pharmacy students' awareness. A total of 102 pharmacy students of the National University of Pharmacy took part in our survey. After professional education, they will carry out pharmaceutical care and consult patients on various issues, including regarding FDI.
4. As the survey has shown, the vast majority of pharmacy students think that food can affect the effectiveness and safety of pharmacotherapy, and 98.0% of students claim that it is important to consider FDIs.
3. About half (49%) of the interviewees claimed that they have enough information about FDI. Knowledge acquired at the university, information from medical representatives of drug manufacturing companies, instructions on the medicine or medication guides were noted as the main sources of information on this issue for them. 98.0% of students claim that it is important to consider FDIs. The vast majority of students (93 %) would like to know more about food-drug interactions.
4. Regarding questions about FDIs, pharmacists demonstrated better knowledge, mainly regarding the interactions of tetracycline with milk, felodipine with grapefruit, MAOI with cheese, spironolactone with potassium-rich food, the timing of administration in relation to food for azithromycin and aspirin. This can be explained by the fact that these cases are well-known examples in literature and special education. But fewer respondents gave correct answers to other questions.
5. The obtained results indicate the inadequacy of pharmacy students' knowledge on a number of issues of the research topic and set the goal of further consideration

of the research results when revising educational and professional programs and improving the content of educational components.

6. The results can be used by education and health care professionals to develop appropriate educational interventions to promote knowledge of clinically relevant FDIs among pharmacists and other healthcare professionals.

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APPENDICES

Appendix A


НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ
МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ
СЕРТИФІКАТ УЧАСНИКА
Цим засвідчується, що
Bourrous Ahlam
Scientific supervisor: Stepanova S.I.
брав(ла) участь у роботі
XXIX Міжнародної науково-практичної конференції молодих вчених та студентів
«АКТУАЛЬНІ ПИТАННЯ СТВОРЕННЯ НОВИХ ЛІКАРСЬКИХ ЗАСОБІВ»
В.о. ректора
Національного фармацевтичного
університету
Алла КОТВІЦЬКА
19-21 квітня 2023 р, м. Харків

Appendix B

PHARMACY STUDENTS' AWARENESS OF FOOD-DRUG INTERACTIONS

Bourrous Ahlam
Scientific supervisor: Stepanova S.I.
National University of Pharmacy, Kharkiv, Ukraine
ahlamtoushaa@gmail.com

Introduction. The irrational use of medicines is a major problem increasingly facing health systems around the world. World health organization (WHO) estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately, and that half of all patients fail to take them correctly. In this regard, the WHO global patient safety challenge "Medication without harm" (2017) has announced to reduce the serious negative consequences of drugs by 50% within 5 years. The drug effect on the human body may differ from the expected one for many reasons. One of them is food-drug interaction (FDI). Food ingredients have the ability to influence the efficacy and toxicity of certain drugs, mainly through their effects on various pharmacokinetic mechanisms (absorption, distribution, metabolism and excretion). Therefore, the knowledge of physicians and pharmacists on the potential FDI is important for safe and effective pharmacotherapy. As evidenced by the literature, several studies have evaluated the knowledge of medical workers on FDI. However, no researches have been conducted among pharmacy students.

Aim of our study is to assess the awareness of pharmacy students on FDI.

Materials and methods. To study the awareness of students of the National university of pharmacy, we worked out the questionnaire and conducted the survey.

Results and discussion. As the survey showed, the majority of pharmacy student think that food can affect the effectiveness and safety of pharmacotherapy, and it is also important to consider the FDI. About half of the respondents claimed that they have enough information about the FDI but almost

90% of them would like to know more about this issue. Students consider that the main information sources on FDI are: professional knowledge acquired at the university, science articles, medication guides and instructions for medicinal products. As for the questions on possible FDIs, the respondents showed better knowledge, mainly on the interactions: tetracycline with milk, theophylline with coffee or tea, felodipine with grapefruit, levodopa with protein food, monoamine oxidase inhibitors with cheese. This may be due to the early discovery, intensive research, and practical use of these interactions, making them well-known examples in the literature and special education.

Conclusions. The results of the study can be considered when revising educational and professional programs and improving the educational components content in the field of health system and for popularizing knowledge about clinically significant FDIs among pharmacists and other medical professionals.

Ф А 2.2.1–32-366

National University of Pharmacy

Faculty for foreign citizens' education
Department of Pharmacology and Pharmacotherapy
Level of higher education master
Specialty 226 Pharmacy, industrial pharmacy
Educational program Pharmacy

APPROVED
The Head of Department
of Pharmacology and
Pharmacotherapy

_____

Sergey Shtrygol'
«21» of September 2022

ASSIGNMENT

FOR QUALIFICATION WORK
OF AN APPLICANT FOR HIGHER EDUCATION

Ahlam BOURROUS

1. Topic of qualification work: «Pharmacy students' awareness of food-drug interactions», supervisor of qualification work: Svitlana STEPANOVA, PhD, assoc. prof.
approved by order of NUPh from "06" of February 2023 № 35

2. Deadline for submission of qualification work by the applicant for higher education: april 2023.

3. Outgoing data for qualification work: publications devoted to the problems of the food-drug interactions, establishing the mechanisms of pharmacokinetic and pharmacodynamic interaction between drugs and food, the influence of drug therapy on the processes of food assimilation.

4. Contents of the settlement and explanatory note (list of questions that need to be developed):
to analyze and summarize literature data on the mechanisms of pharmacokinetic and pharmacodynamic food-drugs interaction; to identify clinically significant and proven common drug-food interactions; to develop a questionnaire; to conduct an anonymous survey, analyze respondents' answers and determine the level of pharmacy students' awareness in the researched issue, find out the attitude of pharmacy students to this problem.

5. List of graphic material (with exact indication of the required drawings):
tables – 4, figures – 7

6. Consultants of chapters of qualification work

Chapters	Name, SURNAME, position of consultant	Signature, date	
		assignment was issued	assignment was received
1	Svetlana STEPANOVA, associate professor of higher education institution of the department of pharmacology and pharmacotherapy	Svetlana STEPANOVA, 21.09.2022	Ahlam BOURROUS, 21.09.2022
2	Svetlana STEPANOVA, associate professor of higher education institution of the department of pharmacology and pharmacotherapy	Svetlana STEPANOVA, 01.11.2022	Ahlam BOURROUS, 01.11.2022
3	Svetlana STEPANOVA, associate professor of higher education institution of the department of pharmacology and pharmacotherapy	Svetlana STEPANOVA, 12.12.2022	Ahlam BOURROUS, 12.12.2022

7. Date of issue of the assignment: "21" of September 2022

CALENDAR PLAN

№	Name of stages of qualification work	Deadline for the stages of qualification work	Notes
1.	Issuance of a task for qualification work; definition of the topic of the work, the goal and task of the research; establishing the object and subject of research; drawing up a calendar plan for work execution	September-October 2022	**done**
2.	Search, analytical processing and accumulation of information sources, practical materials in traditional bibliographic systems and on the Internet; selection of research methods	October-November 2022	**done**
3.	Development of a questionnaire and conducting a survey	November-December 2022	**done**
4.	Evaluation of answers to an anonymous questionnaire among pharmacy students regarding the awareness of food-drug interaction	January 2023	**done**
5.	Analysis and systematization of acquired knowledge, skills and information; assessment of scientific novelty and practical significance of the work	February-March 2023	**done**
6.	Preparation of the manuscript, editing and formatting of the qualification work; preparation of the accompanying documents and submission of work to the Examination Committee of the NUPh.	March-April 2023	**done**

An applicant of higher education _____ Ahlam BOURROUS

Supervisor of qualification work _____ Svetlana STEPANOVA

Ф А2.8-47-110

ВИСНОВОК

Комісії з академічної доброчесності про проведену експертизу

щодо академічного плагіату у кваліфікаційній роботі

здобувача вищої освіти

№ 112849 від « 1 » травня 2023 р.

Проаналізувавши випускну кваліфікаційну роботу за магістерським рівнем здобувача вищої освіти денної форми навчання Буррус Ахлам, 5 курсу, _____ групи, спеціальності 226 Фармація, промислова фармація, на тему: «Обізнаність студентів-фармацевтів щодо взаємодії ліків і їжі / Pharmacy students' awareness of food-drug interactions», Комісія з академічної доброчесності дійшла висновку, що робота, представлена до Екзаменаційної комісії для захисту, виконана самостійно і не містить елементів академічного плагіату (компіляції).

Голова комісії,
професор **Інна ВЛАДИМИРОВА**

3%

28%

Ф А 2.2.1-32-353

REVIEW

of scientific supervisor for the qualification work for the master's level of higher education, specialty 226 Pharmacy, industrial pharmacy

Ahlam BOURROUS

on the topic: « Pharmacy students' awareness of food-drug interactions»

Relevance of the topic. Today, much attention is paid to the problem of irrational pharmacotherapy, because it takes people's lives and leads to disability. In this regard, the WHO global campaign "Medicines without harm" (2017) is designed to reduce by 50% the serious negative consequences of improper use of medicines within 5 years. The effect of the drug on the human body may differ from the expected due to several reasons. One of them is the interaction of drugs with food, drinks and dietary supplements, which are taken together. These interactions range from pharmacokinetic interactions (absorption, distribution, metabolism, and excretion influencing blood levels of drugs) to pharmacodynamic interactions (drug effects). An important aspect of the pharmacist's work is pharmaceutical care. The availability of reliable information on interactions between foods and drugs, on the one hand, and the integration of pharmacist knowledge and experience, on the other hand, will contribute to improving the quality of medical services and safe patient management.

Practical value of conclusions, recommendations, and their validity. The practical value of the results of qualification work is to obtain information that can be considered for modifying of educational and professional programs and improving the content of educational components.

Assessment of work. The literature review is written analytically, in compliance with the requirements of scientific style and the text contains correct references to other authors. The chosen research methods are generally accepted and adequate to the goal and task. The data were processed using traditional statistical methods. A sufficient amount of empirical data for analysis was obtained and

experimental data were carefully analysed. The results of the research were analysed and summarized in comparison with the data of scientific literature and further perspectives and directions of work were highlighted. The work is relevant, meets the requirements and has practical and scientific value. The list of resources for the literature consists of 55 sites. Approbation of research results took place on April 19-21, 2023 at the XXIX International scientific and practical conference of young scientists and students «Topical issues of new medicines development» (Kharkov, Ukraine).

General conclusion and recommendations on admission to defend. The work is performed in full, designed by the current requirements for the qualification works at the National University of Pharmacy, and can be recommended for submission to the State Examination Commission for further defense.

Scientific supervisor _____ Svetlana STEPANOVA

«4» of April 2023

Ф А 2.2.1-32-356

REVIEW

for the qualification work for the master's level of higher education, specialty 226 Pharmacy, industrial pharmacy

Ahlam BOURROUS

on the topic: «Pharmacy students' awareness of food-drug interactions»

Relevance of the topic. Natural foods and dietary supplements have recently become increasingly popular for their roles in medicine and health maintenance. This has, however, led to an increased risk of interaction between prescribed drugs and the bioactive ingredients contained in these foods. These interactions range from pharmacokinetic interactions (absorption, distribution, metabolism, and excretion influencing blood levels of drugs) to pharmacodynamic interactions (drug effects). Pharmacist is the bridge between doctors and patients who counsels and advises the patient to maximize the effect of the drugs and minimize their adverse effects. Therefore, understanding the potential food-drug interactions and their mechanisms is crucial for pharmacists to ensure that patients receive optimal treatment.

Theoretical level of work. The author of the work conducted a comprehensive analysis of theoretical material on the subject of research. The work contains the author's opinion regarding the analyzed provisions and proper argumentation of the author's position. Correct literary references are provided. The theoretical provisions of the qualification work are related to real practical tasks and problems in the field of pharmaceutical care during the dispensing of medicinal products.

Author's suggestions on the research topic. The conducted research made it possible to reveal the level of pharmacy student's awareness regarding food-drug interaction and to conclude that a certain number of aspects in this regard require additional clarification. The obtained results indicate the inadequacy of pharmacy students' knowledge on several issues of the research topic and set the goal of further consideration of the research results when revising educational and professional programs and improving the content of educational components.

Practical value of conclusions, recommendations, and their validity. The author has developed a questionnaire that can be used to assess the attitude and awareness of pharmacists and other healthcare professionals regarding drug-food interactions. The conclusions are well-founded and clear, and correspond to the purpose and objectives of the research. The results obtained can be used by education and healthcare professionals to develop appropriate educational interventions to promote knowledge of clinically relevant food-drug interactions among pharmacists and other healthcare professionals.

Disadvantages of work. No significant shortcomings were identified in the work, however, it can be noted: individual grammatical, stylistic, and technical errors; These do not fundamentally change the assessment of the work and do not reduce its scientific and practical significance.

General conclusion and assessment of the work. The scientific work is done according the requirements for qualification work in NUPh and can be recommended for defense.

Reviewer _____ prof. Natalia POPOVA

«10» of April 2023

МІНІСТЕОТВО ОХОРОНИ ЗДОРОВ'Я
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ
Витяг з протоколу № 14
від 11 квітня 2023 року
м. Харків
засідання кафедри фармакології та фармакотерапії

ПРИСУТНІ: зав. каф. проф. Штриголь С.Ю., проф. Кіреєв І.В., проф. Деримедвідь Л.В, проф. Бутко Я.О., проф. Щокіна К.Г., доц. Бєлік Г.В., доц. Рябова О.О., доц. Жаботинська Н.В., доц. Куценко Т.О., доц. Таран А.В., доц. Матвійчук А.В., доц. Савохіна М.В., доц. Степанова С.І., ас. Кононенко А.В., ас. Толмачова К.С., ас. Цеменко К.В., Адлер Б.А., Чубар`ян Ю.І., Барзак Д.Т., Краснораменська О.В., Шульга Ю.М., Рубан Я.В., Суровцева Д.О., Леонова Я.І., Заворотько Д.І., Вороніна А.О., Давидов Е.М., Шостенко К.В., Дібт Шараф Еддін, Жудат Ікрам, Алауі Абдаллауі Яссін, Буррус Ахлам, Ель Хамді Мохаммед, Меллоукі Хамза, Іфтахі Яссін, Карім Ашраф, Айнау Умайма, Елбадауі Хажар, Ель Хайель Хаджар, Толбі Ель Мехді, Беналлал Зінеб, Бенсаід Мохаммед, Ел-Жамаі Сальма, Ельбахаджі Раіхана, Бензід Ясіне, Кадді Каутар.

ПОРЯДОК ДЕННИЙ:
Розгляд кваліфікаційних робіт здобувачів вищої освіти для подання робіт до Екзаменаційної комісії.

СЛУХАЛИ:
Здобувача вищої освіти Буррус Ахлам зі звітом про проведену наукову діяльність за темою кваліфікаційної роботи: «Обізнаність студентів-фармацевтів щодо взаємодії ліків і їжі».

УХВАЛИЛИ:
Кваліфікаційну роботу розглянуто. Здобувач вищої освіти Буррус Ахлам допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

Завідувач кафедри фармакології
та фармакотерапії, проф. _____ Штриголь С.Ю.
Секретар кафедри фармакології
та фармакотерапії, ас. _____ Кононенко А.В.

Ф А2.2.1-32-042

НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

ПОДАННЯ
ГОЛОВІ ЕКЗАМЕНАЦІЙНОЇ КОМІСІЇ
ЩОДО ЗАХИСТУ КВАЛІФІКАЦІЙНОЇ РОБОТИ

Направляється здобувач вищої освіти Ахлам БУРРУС до захисту кваліфікаційної роботи
за галуззю знань 22 Охорона здоров'я
спеціальністю 226 Фармація, промислова фармація
освітньою програмою Фармація
на тему: «Обізнаність студентів-фармацевтів щодо взаємодії ліків і їжі».

Кваліфікаційна робота і рецензія додаються.

Декан факультету _____ / Світлана КАЛАЙЧЕВА /

Висновок керівника кваліфікаційної роботи

Здобувачка вищої освіти Ахлам БУРРУС у повному обсязі виконала кваліфікаційну роботу. За актуальністю, методичним рівнем, теоретичним та практичним значенням, об'ємом виконаних досліджень кваліфікаційна робота відповідає вимогам і допускається до захисту в Екзаменаційній комісії.

Керівник кваліфікаційної роботи

_____ Світлана СТЕПАНОВА

«04» квітня 2023 р.

Висновок кафедри про кваліфікаційну роботу

Кваліфікаційну роботу розглянуто. Здобувачка вищої освіти Ахлам БУРРУС допускається до захисту даної кваліфікаційної роботи в Екзаменаційній комісії.

Завідувач кафедри
фармакології та фармакотерапії

_____ Сергій ШТРИГОЛЬ

«11» квітня 2023 року

Qualification work was defended
of Examination commission on the
« ___ »__of June__ 2023
with the grade _____
Head of the State Examination commission,
DPharmSc, Professor
_____ / Oleh SHPYCHAK /