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Irrational (Difficult) Prescriptions in Extemporaneous Compounding: Rationing and Preparation

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Abstract

The work represents the data about irrational (difficult) prescriptions in extemporaneous compounding, their rationing and preparation. The given information is released according to the literary data analysis. By studying these literary data, we lead and summarize some examples of irrational (difficult) prescriptions in different medicinal forms.

Extemporal medicines based on the principles of Good Prescribing Practices (GPRP) are the leading criteria for the effectiveness of health systems in the world's leading countries. There is no uniform approach in questions of rationalization of the prescribed medicines in the regulatory sphere of the health care system, has a direct negative influence on the quality and effectiveness of the provided pharmacotherapy.

Material and methods. The part represents information about the works of well-known scientists about the most frequently encountered inconvenient cases of the extemporaneous formulation and the reasons for their formation on individual prescriptions, and possible ways of their elimination.

Results and discussion. Some examples of irrational (difficult) prescriptions presented in literary sources were shown. Difficulties can arise when prescribing medicinal substances that are not soluble in prescribed solvent, at concentrations exceeding their solubility, due to the precipitation of the precipitate in the usual order of their mixing or dissolution, etc. The ability to prepare extemporaneous dosage forms for irrational (difficult) prescriptions with the use of special techniques and to recognize incompatible combinations in prescriptions characterizes the professionalism of pharmacists, prevents possible mistakes and promotes the release of only high-quality extemporaneous medicines to the patient.

The normative substantiation of the problem of pharmaceutical incompatibilities, in our opinion, will increase the professional knowledge of pharmacists about the physical phenomena and chemical interactions that may occur in dosage forms, and will guide them in practical activities in deciding on the choice of a rational method for preparation of the extemporaneous medicine. The analysis of the main approaches to the organization of rational prescribing of extemporal medicines in European countries has shown the need for the introduction of guidelines and standards for health professionals; education and information organizations; conducting monitoring of recipes and prescription drugs; improvement of financial motivation of doctors.

Keywords: irrational (difficult) prescriptions, extemporaneous compounding, rationing, preparation, Good Prescribing Practice

INTRODUCTION

Currently, in medical practice, a significant number of medicines are used, obtained both by synthesis and from materials of plant and animal origin. In addition, their arsenal is rapidly increasing due to the receipt on the pharmaceutical market of newly developed medicines possessing a variety of physical, chemical properties, as well as various pharmacological actions.

At the same time, the effect of medicines in many cases is most effective when applied in various combinations, which causes a relatively high specific gravity in the modern formulation of complex dosage forms containing several ingredients.

A thoughtful combination of several medicinal substances simultaneously often gives a more pronounced therapeutic effect than using them separately. In its composition, the prescription can contain 4-5 or more ingredients (sometimes up to 10-15). Therefore, prescribing a complex composition, the doctor in some cases provides for enhancing the specific effect of the ingredients, in others – weakening or eliminating the side effect of one of the prescribed components.

To achieve the desired therapeutic effect, the phenomenon of antagonism (the opposite effect) of medicinal substances is also used. Thus, it is necessary to pay serious attention to compatibility of medicinal substances in the prescribed extemporaneous medicine [1, 2].

The combination of different medicinal substances in a single dosage form without due regard for their physical and chemical properties, pharmacological action and possible interaction among themselves can lead to the formation of irrational (difficult), or incompatible combinations, which leads to a decrease in their therapeutic effect and the appearance of undesirable side effects.

At the same time, the current state of extemporal recipes, based on the basic principles of Good prescribing practice, is one of the fundamental criteria for the effectiveness of the health care system of developed countries of the world. In this regard, the improvement of prescribing and releasing prescription drugs is the most important priorities of any national health system. The problem is very acute in Ukraine, where at present the recipe does not fully fulfill its functions, first of all social and economic, from the point of view of reimbursing the value of the drug, and often does not correspond to its legal status.

It should be noted that in European countries to prevent unacceptable therapeutic effect of extemporaneous medicine Good Prescribing Practice is used in Europe countries. Moreover, EU emphasizes on what the prescriber should always have in mind as the four aims towards the improvement of Good Prescribing Practice is to:

- maximize effectiveness,
- minimize risks,
- minimize costs,
- respect the patient's choice [9, 10].

The major subjects of GPRP medicines are doctors who have a decisive influence on the choice of drugs. Good

Prescribing Practice is defined by parameters such as the right medicine; on the correct dose; receiving the appropriate time; eligible patients. Nowadays it is the link between doctor, pharmacist and patient.

MATERIALS AND METHODS

Earlier, the terms "irrational (difficult)" and "incompatible" prescriptions were divided and denoted different degrees of unfitness of the medicine. Those who did not have any therapeutic or harmful effect on the patient's body called irrational (difficult) prescriptions.

Incompatible names were those in which, because of the interaction of prescribed medicinal substances with each other or through the body, the therapeutic effect changed in the direction of its decrease, new physical or chemical properties of the medicine appeared. As a result, often form strong effective or poisonous substances adversely affect the body of a sick person.

Rational medicinal prescriptions are divided into compatible, "difficult" and incompatibilities. In turn, incompatibilities are divided into physical, chemical and pharmacological [3, 4].

Knowledge of possible cases of technological difficulties and the formation of irrational (difficult) and incompatible combinations in extemporaneous prescriptions accumulated for many years. They are reflected in the educational and scientific literature of a number of authors [1-6].

In the works of well-known scientists, the most frequently encountered inconvenient cases of the extemporaneous formulation and the reasons for their formation on individual prescriptions are considered, and possible ways of their elimination are indicated. The presence of different sources of these data complicates the work of pharmacists in finding the necessary information to justify the optimal method of medicines preparation.

For example, in Ukraine generalized information on the incompatibilities of individual medicinal substances in the form of a table "Physical and chemical properties of medicinal substances and the features of their introduction into extemporaneous medicines" were first presented in the textbook "Pharmaceutical Technology of Drugs" (professors O. I. Tykhonov, T. G. Yarnykh) and methodological recommendations "Extemporaneous prescriptions. Technology, analysis, usage" [7].

These publications became the methodical basis of the general pharmacopoeial article in the State Pharmacopoeia of Ukraine "Pharmaceutical incompatibilities", which contains five sections and annexes.

As an addendum to this document, the authors also worked to create an electronic information and analytical system "Extemporaneous prescriptions", which will have online access and such sections: information about substances, excipients, compatibility of medicinal substances, etc.

In the United States, basic information on irrational (difficult) extemporaneous prescriptions is presented in the USP Pharmacist's Pharmacopoeia. Articles "1150" "Pharmaceutical Stability" and "1191" "Stability Considerations in Dispensing Practice" contain data on signs of instability in solid, liquid, soft non-sterile and sterile medicinal forms, some examples of irrational (difficult) prescriptions and ways of their possible preparation [8].

The normative substantiation of the problem of pharmaceutical incompatibilities, in our opinion, will increase the professional knowledge of pharmacists about the physical phenomena and chemical interactions that may occur in dosage forms, and will guide them in practical activities in deciding on the choice of a rational method for preparation of the extemporaneous medicine.

In addition, we used the data from literary sources to reflect the results of our work on the regulation of extemporal prescribing, the implementation of Good prescribing practice, which has a positive experience all over the world. Therefore, in the EU countries in the process of rational use of medicinal products, special importance is GPRP.

During studying this problem, were used following research methods: analytical, logical, systematic, content analysis.

Thus, the aim of the study – to lead and summarize some examples of irrational (difficult) prescriptions presented in literary sources as well as an analysis of the main approaches to the organization of the rational prescribing of the medicines in the European countries [1-8].

RESULTS AND DISCUSSION

Irrational (difficult) prescriptions are such combinations of medicinal substances with which the pharmacist, by virtue of his professional knowledge, can prepare a medicinal preparation, resorting to special technological methods.

In this case, it is possible to exclude the incompatibility and release the patient a high-grade and high-quality medicine. Therefore, when you receive a prescription in the pharmacy, you first need to find out the reason for the difficulty in preparing them, and then, choose the appropriate method of technology.

Difficulties can arise when prescribing medicinal substances that are not soluble in prescribed solvent, at concentrations exceeding their solubility, due to the precipitation of the precipitate in the usual order of their mixing or dissolution, etc.

Example No. 1:

Rp.: Anaesthesini 5.0
Acidi borici 3.0
Naphthalani 20.0
Picis liquidae 10.0
Olei Ricini 5.0
Spiritus aethylici 95° ad 100.0
Misce. Da. Signa. For bandages.

20.0 g of naphthalan is insisted for two days in the prescribed amount of 95 ° alcohol, then the alcohol extract is drained, dissolved in it 3.0 g of boric acid and 5.0 g of anestesin, after that, with stirring, castor oil and tar are added.

Example No. 2:

Rp.: Riboflavini 0.001
Solutionis Acidi borici 2 % – 10.0
Misce. Da. Signa. Ophthalmic drops.

In the solution of boric acid, riboflavin dissolves better than in water, so it is first necessary to dissolve the boric acid in the hot water, and then the riboflavin.

Example No. 3:

Rp.: Solutionis Furacilini ex 0.2 – 1000 ml
Novocaini 2.5
Sterilis!
Misce. Da. Signa. Solution for injections.

Furacilin is dissolved in hot water and sterilized by flowing steam at 100 °C for 30 minutes. Then, to the cooled furacillin solution, 2.5 g of novocain hydrochloride is added under aseptic conditions. The concentration of novocain should not exceed 1 %, since at a higher concentration, the color of the solution changes to a brown color. The solution is prepared ex tempore.

Example No. 4:

Rp.: Resorcini 0.6
Pastae Zinci 15.0
Glycerini
Lanolini anhydrici
Aquae Amygdalarum amararum ana 5.0
Misce, fiat unguentum
Da. Signa. Apply to affected areas of the skin.

At the usual order of mixing of medicinal substances, there is a separation of the ointment. Homogeneous ointment is obtained with the following method of preparation: anhydrous lanolin mix with water of bitter almonds, in another mortar mix the powdered resorcinol with zinc paste. The ointments obtained in this way are mixed together and glycerol is added with constant stirring.

Example No. 5:

Rp.: Natrii benzoatis 4.0
Calcii chloridi 5.0
Aquae purificatae 150 ml
Misce. Da. Signa. 1 tablespoon 3 times a day.

An irrational (difficult) prescription that is prepared without agreement with the doctor. If purified water is measured in the vial, concentrated solution of calcium chloride is added, followed by solution of sodium benzoate, a turbidity will appear, followed by the precipitation of a slightly soluble calcium benzoate compound. Therefore, it is rational to first dissolve the ingredients each separately in half the amount of water or dilute their concentrated solutions, and then dissolve the solutions. In this case, the mixture remains transparent.

Tables 1 and 2 show the most typical cases of irrational (difficult) prescriptions that are prepared without and with agreement with the doctor, as well as possible ways to eliminate them.

Table 1: Examples of irrational (difficult) prescriptions that are prepared without agreement with the doctor

Medicines	Causes of difficulties and ways to overcome them
Boric acid solution	Difficult and slightly soluble in cold water substances are dissolved in hot water
Calcium gluconate solution	
Ethacridine lactate solution	
Riboflavin solution 0.02 %	
Furacilin solution (1:5000)	Dissolve in hot water with sodium chloride (0.9 %)
Copper sulfate solution	Poorly wettable large crystals are ground with a small amount of warm water
Potash alum solution	
Solution of hydrochloric acid with pepsin	Change the order of preparation. Pepsin is dissolved in a solution of hydrochloric acid at pH 2.0-3.5
Osarsol solution	To improve the solubility of the osarsol, sodium hydrocarbonate is added as an auxiliary substance
Liniment with menthol, sunflower oil, chloroform	Menthol had better dissolve in chloroform than in oil
Liniment with novocain, chloroform, 10 % ammonia solution	Novocain salt is dissolved in a 10 % solution of ammonia, and then its base in chloroform

Table 2: Examples of irrational (difficult) prescriptions that are prepared with agreement with the doctor

Rp.: Acidi salicylici 2.0 Ichthyoli 10.0 Spiritus aethylici 40 ml Misce. Da. Signa. Rubbing.	Rp.: Iodi 0.1 Kalii iodidi 1.0 Chloroformii 5.0 Olei Vaselini 5.0 Misce. Da. Signa. Rubbing.	Rp.: Mentholi 0.2 Natrii hydrocarbonatis 0.4 Spiritus aethylici 96 % 50 ml Misce. Da. Signa. Rubbing
To dissolve the ichthyol, it is necessary to replace half the amount of ethyl alcohol with ether	Exclude from the prescription potassium iodide, for the dissolution of which it is necessary to add purified water, immiscible with chloroform and vaseline oil	Sodium hydrocarbonate is insoluble in 96 % ethanol, so it is necessary to replace it with 70 % alcohol

Table 3. The Main Approaches to the Improvement of the system of Medical Prescriptions and Prescribing in EU

Country	Presence and leadership standards for health professionals	Education and Information	Monitoring and medical appointments recipes	Financial motivational doctors
Spain, Belgium, Germany, Austria, Netherlands, UK, Sweden	✓	✓	✓	✓
Denmark, Italy, Portugal, Slovakia, Slovenia, Finland, France	✓	✓	✓	
Latvia	✓		✓	
Lithuania, Romania		✓	✓	
Estonia	✓	✓		
Hungary	✓		✓	
Malta	✓			
Poland		✓		
Greece, Ireland			✓	

In European countries, the Good Prescribing Practice is being implemented and improved to address the problem of irrational drug prescribing, which enables people to be provided with effective, high-quality medicines. According to the Good Prescribing Practice, it has been established that the key criteria for the selection of essential drugs (WHO) are: Priority should be given to drugs of proven effectiveness and safety. Unnecessary duplication of drugs and dosage forms should be avoided.

Only those drugs, for which adequate scientific data are available from controlled clinical trials and/or epidemiological studies and for which evidence of performance in general use in a variety of settings has been obtained, should be selected. Newly released products should only be included if they have distinct advantages over products currently in use.

Each drug must meet adequate standards of quality, including when necessary bioavailability, and stability under the anticipated conditions of storage and use. The international nonproprietary name (INN, generic name) of the drug should be used. This is the shortened scientific name based on the active ingredient. WHO has the responsibility for assigning and publishing INNs in English, French, Latin, Russian and Spanish.

The cost of treatment, and especially the cost/benefit ratio of a drug or a dosage form, is a major selection criterion. Where two or more drugs appears to be similar, preference should be given to drugs that have been most thoroughly investigated; drugs with the most favorable pharmacokinetic properties; and drugs for which reliable local manufacturing facilities exist. Most essential drugs should be formulated as single compounds. Fixed-ratio combination products are only acceptable when the dosage of each ingredient meets the requirements of a defined population group and when the combination has a proven advantage over single compounds administered separately in therapeutic effect, safety, compliance or cost [11-14].

A prescription is an instruction from a prescriber to a dispenser. The prescriber is not always a doctor but can also be a paramedical worker, such as a medical assistant, a midwife or a nurse. The dispenser is not always a pharmacist, but can be a pharmacy technician, an assistant or a nurse. Every country has its own standards for the minimum information required for a prescription, and its own laws and regulations to define which drugs require a prescription and who is entitled to write it. Many countries have separate regulations for opiate prescriptions.

In the EU countries, there is existence of Good Prescribing Practice for maximum health satisfaction of their citizens. An increasing number of drugs in the pharmaceutical world and increase growth of diseases, and there has been rapid growth in drug consumption. World Health Organization has estimated that at least one-third of the world's population lacks access to good prescribed drugs.

However, due to the perception of good practice of prescribing drugs as a mechanism of regulation of prescription drugs is the most appropriate definition of the practice in terms of the key principles of the national health systems as the supply of prescription drugs that are safe, effective and affordable. In EU countries good prescribing practice is inappropriate because its lack the necessary requirements. These requirements include, good prescribing and functioning drug regulatory that will help in enforcement. Now pharmacist also contribute to the actualization of GPRP.

An improvement in good prescribing practice refers to the most important priority task of National Health System. The present state of medical recipes based on the principles of effective state regulation GPRP is the main criterion for the effectiveness of health care systems of developed countries. In the EU countries, GPRP is of particular importance to the process of pharmacotherapy, as it allows solving the various issues of the health system. Analysis of the main approaches to the organization of medical formulations and prescriptions drugs that are used in practice to improve medical appointments in Europe, are given in the table 3.

The data in table 3 showed that 23 European countries represented only seven countries using four basic approaches to solving problems of medical formulation, including:

- implementation of guidelines and standards for health care professionals;
- organization of education and information;

- monitoring of recipes and prescriptions drugs;
- financial motivation of doctors.

In the world, there is need to raise issues of introduction of new organizational technologies that contribute to the rational use of medicines. The changes occurring in the field of medicinal products in recent years (imperfect information system and inform professionals about medicines, regulation of appointment and selection in accordance with the standards of care, changes in the rules of prescribing drugs, etc.), are not conducive to rational choice, purpose and the use of drugs in clinical practice. The introduction of the practice of prescribing contributes to the solution of these problems [15, 16].

The most common approach to improving the medical formulation used in 19 (82.6 %) of the 23 countries is to monitor prescription and drug use. This approach is considered in most countries in Europe, as feedback in the medical prescription and medication system between authorized tools (public and public) and health professionals (medical and pharmaceutical workers).

CONCLUSIONS

It should be noted that the ability to prepare extemporaneous dosage forms for irrational (difficult) prescriptions with the use of special techniques and to recognize incompatible combinations in prescriptions characterizes the professionalism of pharmacists, prevents possible mistakes and promotes the release of only high-quality extemporaneous medicines to the patient. Thus, in spite of differences in management and legislation in relation to the monitoring of prescription and drug use in some EU countries, the general principles of the effectiveness of the medical formulation are: coordination and control of appointments; the presence of feedback (mandatory, regular or fragmentary); financial motivation of physicians exercising rational use of medicines.

The results of this study can serve as the basis for taking some important management decisions in the health system of Ukraine in the issues of resolving extemporal formulation problems based on the introduction of Good Prescribing Practice.

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