

УДК 378.14 : 615.072 (477)

DOI 10.11603/me.2414-5998.2018.1.8297

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*I. Horbachevsky Ternopil State Medical University***METHODOLOGICAL ASPECTS OF TEACHING OF STANDARDIZATION OF MEDICINES FOR FOREIGN STUDENTS**

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імені І. Я. Горбачевського МОЗ України”***МЕТОДИЧНІ АСПЕКТИ ВИКЛАДАННЯ СТАНДАРТИЗАЦІЇ  
ЛІКАРСЬКИХ ЗАСОБІВ ІНОЗЕМНИМ СТУДЕНТАМ**

**The aim of the work** – to find ways to solve the main problems faced by teachers working with foreign students in the discipline “Standardization of medicines”; analyze the main issues that can affect the performance of the training of foreign students.

**The main body.** The research is based on the study of materials obtained from open sources of information and authors’ own experience. The article presents modern technologies of teaching and testing of foreign students on “Standardization of medicines”, approved at the Department of Pharmaceutical Chemistry.

Since the quality of the drug is laid down at the stage of pharmaceutical development, the student must clearly know the elements of pharmaceutical development. The purpose of pharmaceutical development is to develop a quality drug and the process of its production, in order to continuously produce products with given functional characteristics and competitiveness in the pharmaceutical market. The future specialist in the pharmaceutical industry needs to learn to choose, in accordance with the pharmaceutical form, analytical methods for controlling the quality of the medicines and make the specifications and be guided in the practical activities of the MCQ on the FDF. Detailed and thorough acquaintance with the basics of the discipline “Standardization of medicines”, gives the opportunity to more fully master the studied material, realize the scientific and creative potential of students, enrich their knowledge, which will be directly used in their practical activities.

**Conclusion.** The proposed method allows the teacher to successfully build an educational process, which ultimately positively affects the overall mastering of the course.

**Key words:** standardization; pharmaceutical development; Pharmacopoeia.

**Мета роботи** – знайти шляхи вирішення основних проблем, з якими стикаються викладачі, що працюють зі студентами-іноземцями при викладанні дисципліни “Стандартизація лікарських засобів”. Проаналізувати основні проблеми, які можуть впливати на результативність навчання студентів-іноземців.

**Основна частина.** Дослідження базується на вивченні матеріалів, отриманих із відкритих джерел інформації та власного досвіду авторів. У статті наведені сучасні технології викладання та тестування іноземних студентів зі стандартизації лікарських засобів, впроваджені на кафедрі фармацевтичної хімії.

Оскільки якість препарату закладається ще на етапі фармацевтичної розробки, студент чітко повинен знати елементи фармацевтичної розробки. Ціллю фармацевтичної розробки є: розробити якісний препарат і процес його виробництва, щоб постійно випускати продукцію із заданими функціональними характеристиками та конкурентоспроможністю на фармацевтичному ринку. Майбутньому фахівцю у фармацевтичній галузі необхідно навчитися вибирати відповідно до лікарської форми аналітичні методи для контролю якості ЛЗ і скласти специфікації та керуватися в практичній діяльності згідно з МКЯ на ГЛЗ. Детальне і ґрунтовне ознайомлення з основами дисципліни “Стандартизація лікарських засобів” дає можливість більш повно засвоїти матеріал, що вивчається, реалізувати науково-творчий потенціал студентів, збагачує їх знаннями, які безпосередньо будуть використані у їхній практичній діяльності.

**Висновок.** Запропонований метод дозволяє викладачеві успішніше будувати освітній процес, що, в кінцевому підсумку, позитивно позначається на загальному засвоєнні курсу.

**Ключові слова:** стандартизація; фармацевтична розробка; Фармакопея.

**Introduction.** The pharmaceutical industry of the European Union maintains high standards of Quality Management in the development, manufacture and control of medicinal products. A system of marketing

authorisations ensures that all medicinal products are assessed by a competent authority to ensure compliance with contemporary requirements of safety, quality and efficacy. A system of manufacturing authorisations ensures that all products authorised on the European

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market are manufactured / imported only by authorised manufacturers, whose activities are regularly inspected by the competent authorities, using Quality Risk Management principles. Manufacturing authorisations are required by all pharmaceutical manufacturers in the European Union whether the products are sold within or outside of the Union. To do this, it is necessary to rationalize the organization of the entire educational process, to improve the content, forms, methods of teaching and learning activity of students of higher educational institutions [1, 2].

**The aim of the work** – to find ways to solve the main problems faced by teachers working with foreign students in the discipline “Standardization of medicines”; analyze the main issues that can affect the performance of the training of foreign students.

**The main body.** The research is based on the study of materials obtained from open sources of information and authors’ own experience. The article presents modern technologies of teaching and testing of foreign students on “Standardization of medicines”, approved at the Department of Pharmaceutical Chemistry.

The aim of the subject “Standardization of medicines” follows the goals of educational and professional training programs for graduates of Higher Medical Education Institution and is determined by the content of the systematic knowledge and skills that a pharmacist must comprehend. The knowledge that students receive during study the subject is the basis for block of subjects that provide professional and practical training. “Standardization of medicines” as a subject is based on previously studied by the students subjects such as “Pharmaceutical Chemistry”, “Drug technology”, “Pharmacognosy”. The subject “Standardization of medicines” is studied by the students on the 5th year in the 9th semester.

The study of the standardization of medicines forms in students a complete picture of the different quality indicators for assessing the quality of medicines depending on the type of dosage forms; the development of quality control methods, using pharmacopoeial methods of analysis that are used for quality control of finished medicinal products; quality guidelines and other regulatory documents that ensure the appropriate level of finished medicinal products’ quality, provide the fundamental knowledge and practical skills for future career of a pharmacist.

Lectures cover basic theoretical material of particular or more topics of the discipline, reveal the main issues of the relevant chapters of the discipline. Practical classes (seminar classes) envisage a detailed study

by the students of some theoretical principles of the subject with the lecturer and the formation of ability and skills to their practical use by a student’s individual performance of various tasks and solving computational problems.

Students’ individual work involves mastering an educational material, such as an independent study of particular topics of the subject at the time free from mandatory training classes, and provides preparation to all types of control. Educational material of the subject that is envisaged by a curriculum for learning by the students during independent work is submitted for final control along with educational material that was worked up during the classes.

Consultations (individual or group) are conducted to help students to understand and explain complicated issues for self-understanding, to solve complex problems arising during the independent learning of educational material in preparation for the practical trainings, or before differential credit. Matricula is considered to be passed when the student with full knowledge of the techniques independently, in strict sequence of work, performed practical skills and formulated conclusions competently. During the performing practical skills the lecturer has the right to direct the student who makes small errors and minor mistakes in carrying out the work. Matricula is considered not to be passed when the student knows the actual material, shows ignorance of the techniques, inability of practical skills, makes gross errors in the sequence of work and the formulation of conclusions.

Semester differential credit – it is a form of final control, which is to assess the mastering of educational material by a student on specific subject on the basis of the results of the individual tasks performed and checking of mastering an educational program by a student.

Drug manufacturing control requires high level and intensive analytical and chemical support of all stages to ensure the drug’s quality and safety. The pharmacopeia constitutes a collection of recommended procedures for analysis and specifications for the determination of pharmaceutical substances, excipients, and dosage forms that is intended to serve as source material for reference or adaptation by anyone wishing to fulfill pharmaceutical requirements. The most important analytical technique used during the various steps of drug development and manufacturing is the separation technique: High Performance Liquid Chromatography (HPLC).

Drug development starts with the discovery of a molecule with a therapeutic value (fig. 1). This can

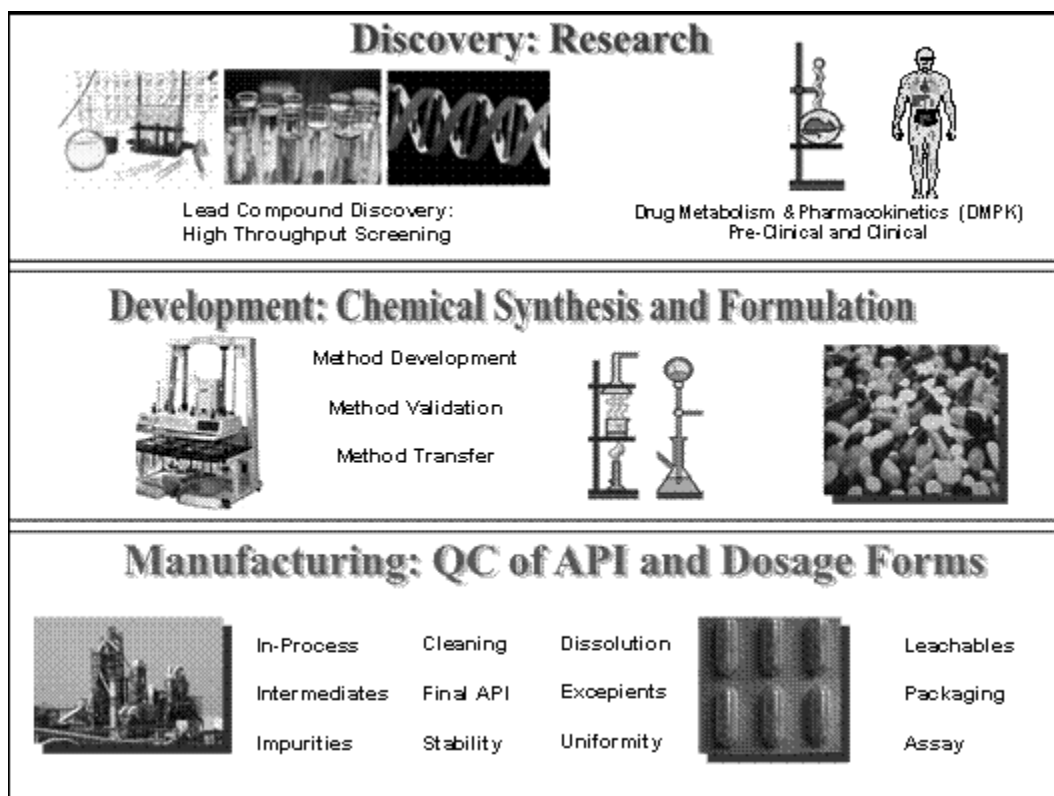


Fig. 1. Drug development.

be done by high throughput screening during which separations by fast or ultra-fast HPLC are performed. At the discovery stage there can be also characterizing synthetic or natural products. Drug metabolism and pharmacokinetics is the step where the candidate compounds for drug are tested for their metabolism and pharmacokinetics. The studies involve use of LC-MS or LC-MS/MS [3, 4].

The next stage is the development stage, where HPLC is used to characterize products of the chemical synthesis, by analyzing the active pharmaceutical ingredients (API), their impurities and/or degradation products generated by accelerated aging. The development of formulation requires also studies of the dissolution properties of solid dosage forms as well as assays of the pharmaceutical formulations. Method for the verification of system's cleanliness during the manufacturing process are developed and used at this stage. All the HPLC methods that have been finalized at the developmental stage are validated and transferred to the manufacturing laboratories for a quality control analysis.

During the last decade parallel synthesis of potential lead compounds, using combinatorial chemistry, has been done. The large numbers of products created by the combinatorial chemistry are then identified by fast LC-MS methods and screened by in-vitro bioassays

and/or pharmacological or chemical tests to allow a selection of a few chosen drug candidates.

When the lead compounds are selected, the next steps involve pharmacological studies. Due to its high sensitivity and selectivity, HPLC coupled with tandem mass spectrometry, HPLC-MS/MS, has become the predominant method in bioassays, and pharmacokinetic and metabolic studies. In addition, another new development in this field has been the introduction of column's packing with ultra-fine particles (<2  $\mu\text{m}$ ) enabling short columns to be used (5 cm or less) and rapid analyses (e.g., 5 min or even less than 1 min) to be carried out by UPLC (ultra performance liquid chromatography).

The support of bioanalytical testing includes quantitation of a target compound in various biological matrices as part of preclinical lead optimization by measurement its adsorption, distribution, metabolism and excretion. The samples are physiological fluids such as plasma, serum, tissue extracts and urine, typically from experimental animals or human subjects. During the last decade conventional HPLC methods using fluorescence or electrochemical detection, following an elaborate sample clean-up, have been replaced by HPLC-MS/MS or UHPLC-MS/MS methodologies. Sample clean-up is simpler and more automated and

usually involves protein precipitation and/or solid phase extraction techniques.

The chromatographic method is typically very rapid, gradient or isocratic, using small columns' dimensions, such as 2.1x50 mm or less. A trace of a typically stable daughter ion signal, obtained from the fragmentation of a parent analyte is used for the detection and quantitation. Such a mode is called MRM (multiple reaction monitoring) or SRM (selective reaction monitoring), which is more stable, sensitive and selective than either the fluorescence or electrochemical signal. Samples are usually ordered in 96 microplates for higher throughput and minimum variability of the sample vials. An internal standard is used typically to minimize assay variability, due to the clean-up stage and MS/MS response, which is still less stable than UV response.

All HPLC methods used for the development of pharmaceuticals and for the determination of their quality have to be validated. In cases whereby methods from the Pharmacopoeia's are used, it is not necessary to evaluate their suitability, provided that the analyses are conducted strictly according to the methods' intended use. In most other cases, especially in cases of modification of the drug composition, the scheme of synthesis or the analytical procedure, it is necessary to re-evaluate the suitability of the HPLC method to its new intended use.

The parameters tested throughout the method validation as defined by the ICH, USP and FDA and other health organizations are the following: specificity or selectivity, precision, accuracy, linearity range, limit of detection, limit of quantitation and robustness.

All these aspects students study in the subject "*Standardization of medicines*". As a result of study the subject "Standardization of medicines" a student should know: structure of the European (British) Pharmacopoeia; normative documents relating to the quality of medicines (guidelines, regulations, specifications, technical specifications, etc.); theoretical fundamentals of pharmacopoeial analysis methods; practical application of pharmacopoeial analysis methods in professional activities; the main quality indicators for assessing the quality of finished medicinal products depending on the type of dosage form; primary and secondary pharmaco-technological parameters by which quality

of medicines is assessed; types of specifications and their use for professional activities; validation characteristics during the validation of analytical methods; the structure of the quality control methods.

Teachers are constantly working on improving the necessary teaching and methodological support of the discipline, they seek to acquire knowledge, practical skills, contribute to the formation of scientific outlook, moral, aesthetic and other personal qualities, and the education of the team. They also focus on the needs of the student in certain knowledge, skills and abilities, based on further self-education, since the formation of the personality of a specialist does not end in an educational institution; it lasts for a lifetime during practical activity and continuous improvement of professional skills.

In countries of Middle East undergraduate students do not study "Standardization of medicines" but postgraduate students study subject "Pharmaceutical quality control and good laboratory practice" in Master in Quality control and drug analysis. In this course, the basic concepts and philosophies of quality are discussed. Quality management systems and standards such as TQM, ISO, GMP is also included. In addition to statistical process control, quality control charts, process capability analysis, acceptance sampling plans and military standards are covered. This course also covers the quality assurance programs applied in pharmaceutical practice and validation of these programs. Control programs for raw materials, in-process and finished products are discussed. Sampling and sampling programs, record handling and documentation are also included. So in our opinion, undergraduate students must study subject which will prepare them for "Pharmaceutical quality control and good laboratory practice" and this subject is "Standardization of medicines".

**Conclusions.** To prepare the students, studying the discipline "Standardization of medicines", integrating the laws and methods of many sciences, plays an important role in this discipline. It is a discipline that preserves the quality of medicines, and hence the health of the people. It allows students to systematize knowledge and practical skills and use them in their professional activities.

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Received 27.09.17

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