Teaching and practice of pharmaceutical comprehensive study in China

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Abstract: Pharmaceutical comprehensive study (PCS) is a new system of experimental teaching in China, which integrates multidisciplinary pharmaceutical knowledge and covers the basic process of new drug discovery. To explore the feasibility of this experiment teaching system and mode, we developed PCS as an elective course. The PCS is designed with two sections: pharmaceutical comprehensive design (PCD) and pharmaceutical comprehensive experiment (PCE). The PCD section includes literature review, comprehensive project design and oral examination. PCE can be divided into four parts: synthesis, quantitative determination, pharmacodynamic evaluation, and formulation and quality determination. Course grade was determined by experimental performance, written report, literature review, new project design and oral examination. The learning interest, experimental ability, theoretical level and literature retrieval ability, team spirit and interpersonal skills have been all significantly improved among students taking this course. A survey was administered at the end of the semester to the enrolled students. The responses were reported as percentages, and the feedback was positive. The course was highly recommended by the teaching inspection committee. This new course plays an important role in developing students' creativity and comprehensive ability. It could help students understand the focus and features of every secondary discipline, as well as establish scientific and reasonable knowledge system. Most students can better understand the process of drug research after this course.

Keywords: Pharmaceutical comprehensive experiment; Undergraduate; Multidisciplinary; Pharmaceutical sciences; Experiment teaching

CLC number: R192 **Document code:** A **Article ID:** 1003–1057(2019)3–209–07

1. Introduction

In China, pharmaceutical sciences can be divided into many disciplines, such as medicinal chemistry, natural medicinal chemistry, pharmaceutical analysis, pharmacology, pharmaceutics, clinical pharmacy, pharmacy administration and so on. These disciplines are called secondary disciplines of pharmaceutical sciences. Students will find jobs in relevant organizations, such as pharmaceutical companies, hospitals or the China Food and Drug Administration, after their graduations. This article introduces the current situation and reforms of undergraduate pharmaceutical experiments in Peking University.

The freshmen majoring pharmaceutical sciences at our school will take introductory courses, such as advanced mathematics, general physics, general chemistry, analytical chemistry, general biology and English. Such basic knowledge will support the rest of the program. Students begin to learn the knowledge of above-mentioned secondary disciplines of pharmaceutical sciences in their sophomore year. At the same time, they also need to do experiments related to these courses, such as experiments in organic chemistry,

Received: 2019-01-15; Revised: 2019-02-28; Accepted: 2019-03-01.
Foundation item: The Education and Teaching Research Project of Peking University Health Science Center.
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http://dx.doi.org/10.5246/jcps.2019.03.021

physical chemistry, medicinal chemistry, natural medicinal chemistry, pharmaceutical analysis, pharmacology and pharmaceutics.

Although there are many lab courses and these courses have been run for many years, there are still problems. First, these lab courses are spread out in different semesters and taught by different teachers in related disciplines. Spreading the classes causes loss of consistency and makes it hard for students to integrate the knowledge between disciplines. Second, the experimental content in every course is independent, and there is no connection among the experiments. Third, without participating in the experimental design, students may lack the motivation of simply performing the experiment. For these reasons, students may only learn the skill that already exists in the lab course experiments and do not get the integrated picture and role of each stage, including the improvement of comprehensive quality and innovative ability[1,2].

Pharmaceutical science is a multidisciplinary area, which includes biology, chemistry, physics and informatics, to name a few[3,4]. Due to the higher demands on the pharmaceutical professionals with comprehensive ability and creativity, pharmaceutical comprehensive study (PCS) has recently been launched at Peking University with the goal of solving the problems mentioned above. It's a new pharmaceutical experimental teaching system that integrates knowledge of multiple secondary disciplines of pharmaceutical sciences. Students can choose one classical drug for this course and do the synthesis or extraction of the drug first, determine its quality and pharmacology activity, and then make formulations[5]. This course has the following advantages[6]. First, students will have an overall understanding of pharmaceutical sciences and the process of drug research. Second, students will benefit from the disciplinary cross-over and integration, and will learn more about the relationship and feature of each secondary discipline. Third, the contents are not a simple gathering of existing experiment schemes. On the contrary, they are innovative and combinations of green chemistry and environmental protection idea. Fourth, there is no other course that offers independent research design, which will improve the comprehensive ability of students in areas such as literature searching, writing, cooperation and presentation skills. In summary, this integrated course will give students a broader understanding, thereby preparing them to effectively contribute intellectually and experimentally.

2. Methods

The PCS can be summarized in to two sections: pharmaceutical comprehensive design (PCD) and pharmaceutical comprehensive experiment (PCE) (Fig. 1).

In PCD section, students are required to do literature review and design a comprehensive project. This can be about the improvement of the existing projects or design of new comprehensive experimental project. On one hand, this section can provide materials for new comprehensive experimental project; on the other hand, it can foster the development of students' scientific thinking to make them realize that only with the combination of theory and practice can they obtain comprehensive knowledge and research skills. Finally, oral examination is given to evaluate their understanding of the pharmaceutical research. All students should present their newly designed comprehensive experimental projects in detail. We will discuss the problems that may exist in the design, share experiences and put forward suggestions and opinions for the improvement of the course. This section takes 40% of the grade.

The PCE section takes 60% of the grade. Here, we discussed the PCE portion using the Aspirin project as

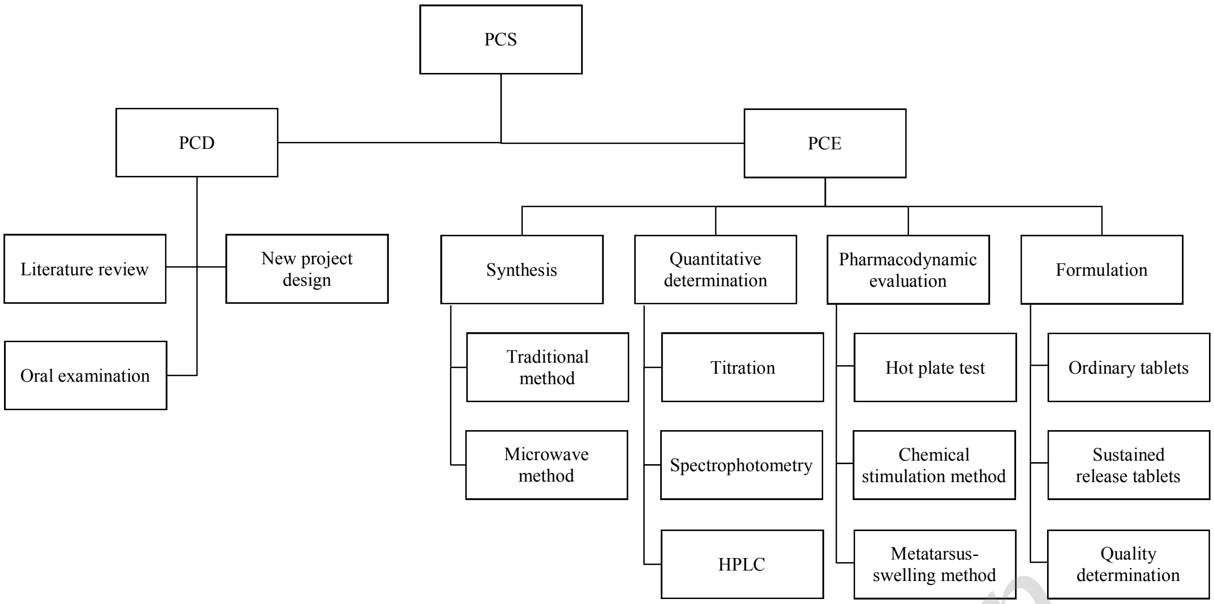


Figure 1. PCS illustration (using Aspirin project as an example). PCS includes PCD and PCE. PCE includes literature review, new project design and oral examination. PCE has four parts: synthesis, quantitative determination, pharmacodynamic evaluation and pharmaceutic formulation. Each part in PCE has 2–3 different methods.

an example. The project can be divided into four parts: synthesis, quantitative determination, pharmacodynamic evaluation, preparation and quality determination of aspirin tablets (Fig. 1).

The first part involves synthesizing raw materials using chemical reagents or extracting and separating active ingredients from traditional Chinese medicines or natural drugs. For example, in the Aspirin project, both traditional and microwave methods have been used. Students can not only consolidate the original knowledge and master the emerging microwave technology which presents the green chemistry trend of pharmaceutical experiments, but this will also allow the students to realize the strengths and weaknesses of both methods.

The second part would be getting information about the quality of the product through analytical techniques, then optimizing synthetic routes and processes to prepare qualified raw materials or active ingredients. Three main methods in pharmaceutical analysis, titration, spectrophotometry and HPLC, have been used to determine the purity and content in the Aspirin project. Knowledge in every independent experiment and related theoretical course has been connected together in this section. In this way, students will have a deeper understanding of the role that analytical techniques plays in pharmaceutical sciences.

The third step involves evaluating the pharmacological effect of the raw material or active ingredient by analyzing its pharmacodynamic and pharmacokinetic properties at the cellular or whole animal level. The hot plate test and chemical stimulation methods have been used to determine the analgesic effect of Aspirin, while the rat metatarsus-swelling method has been used for anti-inflammatory experiments. Students could observe different effects caused by different drug concentrations and master the basic operation methods of an *in-vivo* pharmacological experiment, such as capturing, marking and weighing the subject, as well as oral gavage administration, intraperitoneal injection and sacrifice methods for both mice and rats. Students may have a better understanding and grasp of pharmacology skills in this way.

The final step includes making formulations from the above-mentioned raw material or active ingredients, determining the quality of the formulation and improving the prescription process, finally forming a rational designed formulation with stable quality, which is also called the target product. In the Aspirin case, the preparation of ordinary tablets *vs.* sustained release tablets, and the comparison of their appearance, tablet weight difference, hardness, friability and dissolution make students understand the importance of pharmaceutics and formulation in drug research.

The design of the integrated project is more than the sum of its parts. It's the relationship between those parts and the application of a proper academic philosophy that allow to be more valuable than its constituents[7]. Multiple experimental methods have been designed in parallel for each part. The use of different methods toward the same goal not only allows students to realize the application scope of each method, but also shows them the dialectical way of thinking that there is not only one method in solving a problem and each method has its advantages and disadvantages.

In China, most of the courses are primarily given by lecturing, and there is a lack of interaction between the students and teachers. The teaching mode in PCS combines lectures, classroom discussion, experiments and oral examination. Interactions between teachers and students have been established in this way. The teaching target population for this course in Peking University is students of pharmaceutical sciences in the fourth year of the study. Students can take this as an elective course. The associated teaching materials have been developed by us.

3. Results

The contents of this course are coherent and correlated with each other. For example, in an analytical experiment, students do not know how a white powder is made for quantitative determination, whereas they make the study material by their own in this course. In this way, the learning interest and practical ability can been improved.

During the process of writing reports and reviews, students will consult much literature. They will also think deeply and put forward the improvement measures or other possible solutions for the problems encountered in the experiments. As parallel experiments have been designed in every section, students will make detailed comparisons of different experimental methods to analyze their advantages and disadvantages, as well as their applications. This process can significantly improve their understanding of the knowledge and literature retrieval ability.

There are both independent and group experiments in the course. This grouping method could help students improve the teamwork spirit and interpersonal skills.

Our survey shows that students fully support the establishment of this course. The course helps students systematically gain experience over various disciplines. More importantly, it makes students have an overall understanding of the process of drug research through the integration of multiple subjects.

The adoption of parallel experiments using various techniques helps students realize the strengths and weaknesses of different methods, thus helping them understand the principle and application range of each method more intuitively and firmly. It would also set the stage for the selection of experimental methods in future research work.

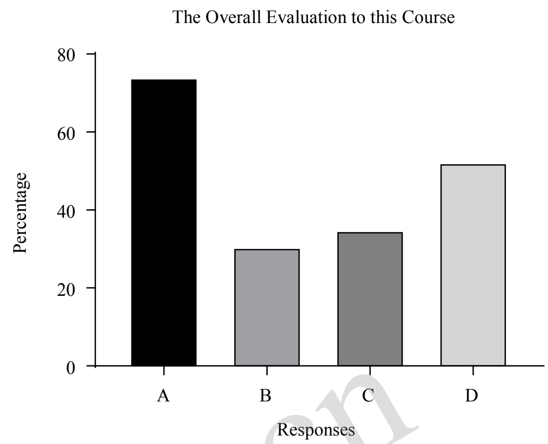
To gauge student perception of the new course, a survey was administered at the end of the semester, which was the basis for changes in subsequent years. Out of the 28 students enrolled in the course over the two academic years (2014–2016), 23 students completed the survey for a response rate of 82%.

In summary, more than 91% of students were satisfied with this course, and none responded with dissatisfaction. Moreover, 74% of students deemed that it was indeed necessary to establish this course, 30% were interested in the contents of this course, and 35% agreed that the design of the course was reasonable and the content was novel. In addition, 52% thought this course covered a wide range of knowledge (Fig. 2).

For the student responses to the features of this course (Fig. 3), 65% agreed that comprehensive experiments had a higher requirement on comprehensive capacity, and the harvest was greater at the same time. Moreover, 83% believed that this course could help them integrate the relevant knowledge that they had learned before and agreed that it was a great help for them to improve their comprehensive ability. In addition, 52% considered that this course required higher operation skills, and it was important so they could improve. Furthermore, 78% believed that the knowledge in this course had both coherence and relative independence, which could enhance learning interest and improve comprehensive qualities.

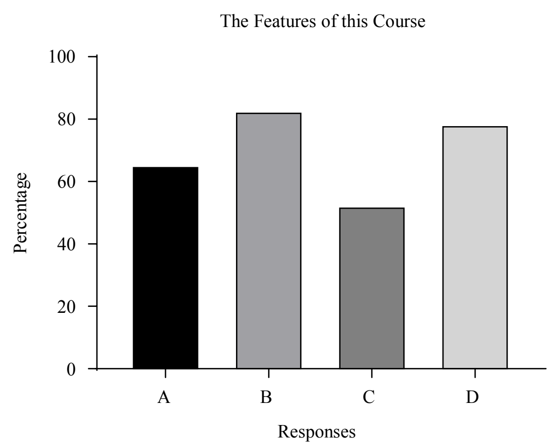
Regarding the assessment mode, 70% of student agreed that it helped them better understand the knowledge dispersed in every sub-discipline. Moreover, 78% believed this mode improved their capabilities of experimental design, analyzing and solving problems. In addition, 44% thought this mode enhanced the literature retrieval and thesis writing abilities. Furthermore, 57% considered oral examination was a great help for their language organization ability. Besides, 30% thought this mode was more difficult than the traditional assessment mode that only had an experimental part (Fig. 4).

Briefly, 81% of students were in agreement for the necessity of cooperation, and others responded neutrally. Moreover, 57% thought this course should be taken in the third year, 30% thought it would be better in the fourth year, and 8.7% said any year was acceptable (Table 1).



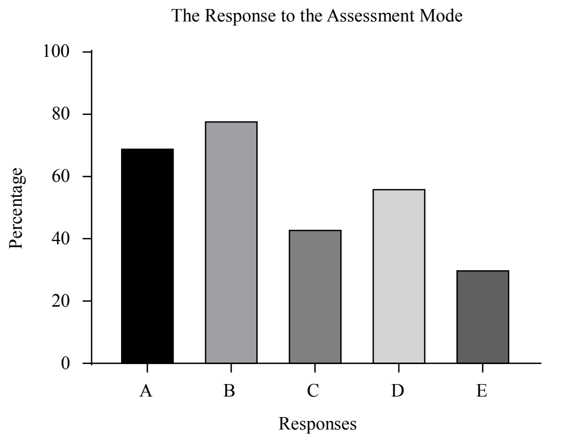
A. It was necessary to set up this course (73.9%);
B. I am interested in the contents of this course (30.4%);
C. The design of the course was reasonable and the content was novel (34.8%);
D. It covered a wide range of knowledge (52.2%).

Figure 2. The overall evaluation to this course. More than 91% of students were satisfied with this course, and none responded with dissatisfaction.



A. This course had a higher requirement on comprehensive capacity, and at the same time achievement was greater (65.2%);
B. This course helped me integrate the relevant knowledge which I have learned before and improved my comprehensive application ability (82.6%);
C. This course required higher operation skill and it was important to the improvement of operation skill (52.2%);
D. The knowledge in this course had both coherence and relative independence which could enhance learning interest and improve comprehensive quality (78.3%).

Figure 3. Student responses to the features of this course. This course helped students integrate the relevant knowledge, improve the comprehensive application ability and operation skill, enhance learning interest and improve comprehensive quality.



A. It helped me better understand the knowledge dispersed in every subdiscipline (69.6%);
B. It helped me improve the capacity of experiment design, analyzing and solving problems (78.3%);
C. It helped me enhance my literature retrieval and thesis writing abilities (43.5%);
D. Thesis defense was a great help in their language organization (56.5%);
E. It's more difficult than the traditional assessment mode (30.4%).

Figure 4. Student responses to the assessment mode. The assessment mode of "literature review + experiment + oral examination" helped students better understand the knowledge dispersed in every sub-discipline, improved their capacities of experiment design, analyzing and solving problems, enhanced the literature retrieval, thesis writing abilities and language organization ability.

Table 1. The survey about the necessity of cooperation and course time.

	Responses	%
The necessity of cooperation	Very necessary	60.8
	Necessary	21.7
	Just as well	17.4
	No need	0.0
The course time	The first year	0.0
	The second year	4.4
	The third year	56.5
	The fourth year	30.4
	All OK	8.7

The enrollment is increased from 10 students of the first year to 18 students of the second year. This demonstrates that students are interested in this course. The teaching inspection committee of our school commented on this course after their inspection. They think PCE is a course which can help students understand the overall process of drug research systematically and improve their comprehensive ability. Therefore, this course has great potential and deserves recognition.

During the course, we found that the operational skill of students at the pharmacology part is weak compared with other parts. We had to teach the students how to do oral gavage and intraperitoneal injection step by step. This indicates that they don't have enough experience in this area, and more training should be given when they take the pharmacology lab course in their third year. Therefore, this course also plays a guiding role for other curriculum optimization.

4. Conclusions

PCS covers the general process of drug development from drug synthesis, quality analysis, pharmacological evaluation, to formulation and quality determination. It provides the opportunity for students to practice the related experiments with regards to pharmaceutical research, and design new projects independently. It helps students realize the focus and features of every secondary discipline, improve their abilities of literature review and oral presentation skills, and establish scientific and reasonable knowledge systems. The knowledge from different subjects, which the students learned from the experiments, can be connected together and help students have a broad understanding of drug discovery. The student-designed projects in the PCD section in the current semester could be further tested on their feasibility and added into the course in the coming term. Independent experiments cannot achieve these results.

We did pre-course work for this project for about 6 months before we established this course, and we have run the project for about 2 years. Our university provided a lot of support for the course in terms of lab space, manpower and funding. Teaching spaces that can be used for all the experiments are necessary for the course. We have professionals who are familiar with those experiments and technicians who can maintain the equipment. The university also gave us some funding for the reform of education and teaching research projects to buy the equipment and materials that are needed in the course. In general, this mode could be easily translated or used for the programs which focus on drug research in other universities around the world.

Acknowledgements

The authors are thankful to Ester Fernandez-Salas, Angelo Aguilar, Zhaomin Liu and Caroline Foster in University of Michigan, Xuezhi Feng, Hongyan Zhang, Ting Yu, Jun Yang, Hua Liu and Yan Lu in Peking University for their assistance and support in this work.

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中国药学综合性实验教学与实践

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摘要: 药学综合性实验整合多个学科的药学知识, 覆盖新药研发的基本流程, 是中国实验教学的新体系。我们为探索该实验教学模式和体系的可行性, 以限选课的形式开设了药学综合性实验课程。本课程分为药学综合性实验设计(PCD)和药学综合性实验(PCE)两部分。PCD部分包括文献综述、综合性实验设计及展示。PCE部分包括合成、含量测定、药效学研究, 制剂及其质量评价。课程成绩由实验操作、报告、综述、综合实验设计及展示等部分成绩组成。该课程对学生的学习兴趣、实验技能、理论水平和文献查阅能力、团队合作精神及人际关系均有明显提高。学期末我们对该课程进行问卷调查, 得到学生的正面反馈, 学院教学督导委员会也对本课程的开设给予了充分的肯定。本课程对培养学生的创新能力及综合素质具有重要作用, 可以帮助学生理解每个二级学科的特点, 构建科学合理的知识体系, 增强对药物研发过程的整体理解。

关键词: 药学综合性实验; 本科生; 多学科; 药学; 实验教学