医薬品相互作用研究
一　般　論　文
43(1) 17-23（2019）

Questionnaire survey on knowledge and perceptions of generic medicines for pharmacy students

Tomohiko TAIRABUNE[1*], Takeshi CHIBA[1], Takashi TOMITA[1], Tomoya SAKURADA[2], Eriko KOBAYASHI[2], Nobunori SATOH[2], Kenzo KUDO[1]

[1]Division of Clinical Pharmaceutics and Pharmacy Practice, Department of Clinical Pharmacy, School of Pharmacy, Iwate Medical University
[2]Department of Social Pharmacy, Graduate School of Pharmaceutical Sciences, Chiba University

（Received May 11, 2018; Revised September 29, 2018; Accepted November 27, 2018）

In pharmaceutical education, students must be given basic knowledge of generic medicines and the needs of promoting their use. In this study, we compared the knowledge and perceptions of generic medicines among 3rd to 6th year students in the Faculty of Pharmaceutical Sciences. A total of 626 students completed the questionnaire (response rate of 98.6%), including 150 in 3rd year, 162 in 4th year, 162 in 5th year, and 152 in 6th year. Overall, very few students in all years answered correctly "80 to 125%" when asked to give the acceptable tolerance range at a 90% confidence interval of the mean blood concentration ratio of a generic medicine and a brand-name medicine in bioequivalence studies. The 4th to 6th year students were significantly more likely to answer "agree" to the questions "I have been introduced to issues on the bioequivalence of generic medicines during my pharmacy education " and "Generic medicines are less expensive than brand-name medicines" than the 3rd year students. On the other hand, compared to 3rd year students, 4th and 5th year students were significantly more likely to answer "disagree" for questions suggesting that generic medicines are of inferior quality, less effective, and produce more side effects than brand-name medicines. Based on these results, to promote the use of generic medicines, it is necessary for pharmacy students to be educated about how to evaluate bioequivalence studies for generic medicines.

Key Words: generic medicines, questionnaire survey, pharmacy students, bioequivalence

Introduction

The Japanese government has promoted the use of generic medicines in order to minimize the increase in national medical expenditure due to its aging population and changes in medical technologies. As result, the rate of generic medicine use has increased over the past several years, reaching 66.8% in 2016[1]. Despite these increases, the Ministry of Health, Labour and Welfare in their "Basic policy 2015 of the economic financial administration and reform" set the target value of the quantity share as 80% as early as possible until the end of fiscal year 2020[2]. Therefore, further promotion of the use of generic medicine is necessary in the future. To achieve this goal, the Ministry of Health, Labour and Welfare created "the road map for further promotion of use of the generic medicine," which includes "improvement of the understanding of generic medicines in medical and pharmacy education" [3]. In other words, to promote of using generic medicines, it is important to ensure that pharmacy students have sufficient knowledge and perceptions of generic medicines.

Generic medicines, containing the same amount of active ingredients as their equivalent brand-name medicine, are given at the same dosages and route of administration, then overall have the same therapeutic effect. However, some studies have indicated that generic medicines do

[1] Division of Clinical Pharmaceutics and Pharmacy Practice, Department of Clinical Pharmacy, School of Pharmacy, Iwate Medical University　2-1-1 Nishitokuta, Yahaba-cho, Shiwa-gun, Iwate 028-3603, Japan
[2] Department of Social Pharmacy, Graduate School of Pharmaceutical Sciences, Chiba University　1-8-1 Inohana, Chuo-ku, Chiba-shi, Chiba 260-8675, Japan
*Corresponding author: tomohiko tairabune
E-mail: tomohiko.tairabune@j.iwate-med.ac.jp

differ from brand-name medicines in terms of clinical effect and quality[4-6]. In response to these studies, the Ministry of Health, Labour and Welfare has begun publishing information on the quality of generic medicines[7] to ensure reliability of their quality. Having an appropriate understanding of generic medicines is essential to carrying out further promotion of generic medicines in the future, so it is important to enrich education on generic medicines for undergraduate pharmacy students. Currently, however, pharmacy students' level of knowledge and actual perceptions of generic medicines are unclear.

The aim of this study was to explore pharmacy students' knowledge and perceptions of generic medicines via a questionnaire survey. These results can then be utilized in planning pharmacy education for generic medicine.

Methods

1. Questionnaire survey

Questionnaires were administered to 3rd to 6th year students of Faculty of Pharmaceutical Sciences, Chiba University and School of Pharmacy, Iwate Medical University from April 1 to June 30, 2015. Questionnaires were distributed to students directly and collected immediately after completion. The purpose of this survey and the confidentiality of personal information were described in the questionnaires (Fig.1).

Q1. Please select your sex.
1. Male
2. Female

Q2. Please select your grade at your university.
1. 3rd year　2. 4th year
3. 5th year　4. 6th year

Q3. Please state your age.
(　　) years

Q4. Before entering the Faculty of Pharmacy, did you graduate from a university, junior college, or vocational school?
1. Graduate master's course
2. Graduate doctoral course
3. University
4. Junior college
5. Vocational school
6. High school

Q5. Do you know what "bioequivalence" is?
1. I understand the meaning of bioequivalence.
2. I know of bioequivalence.
3. I don't know.

Bioavailability is proportion of the unchanged or active metabolite of the active ingredient that enters systemic circulation. According to the Ministry of Health, Labor and Welfare, "bioequivalence" is defined as when the ratio of the bioavailability of a generic medicine to that of a brand-name medicine is within the tolerance interval.

Q6. Bioequivalence means that the 90% confidence interval for the ratio of AUC (area under the plasma drug concentration) and Cmax of the generic medicine to those of the branded medicine is within a certain tolerance range. Please select the applicable range.
1. 80 - 120 %
2. 80 - 125 %
3. 90 - 100 %
4. 95 - 100 %
5. 95 - 105 %

Q7. Please read each question and select the number that best represents your opinion.

		Strongly agree	Agree	Neutral	Disagree	Strongly disagree
a	All generic products of a particular medicine rated as generic equivalents are therapeutically equivalent to the brand-name medicine	5	4	3	2	1
b	All generic products of a particular medicine rated as generic equivalents are therapeutically equivalent to each other	5	4	3	2	1
c	I have been introduced to issues on the bioequivalence of generic medicines during my pharmacy education	5	4	3	2	1
d	I need more information on how bioequivalence studies are conducted for generic medicines	5	4	3	2	1
e	A generic medicine must be in the same dosage form (e.g., tablet, capsule) as the brand-name medicine	5	4	3	2	1
f	A generic medicine must contain the same dose as the brand-name medicine	5	4	3	2	1
g	Generic medicines are inferior in quality than brand-name medicines	5	4	3	2	1
h	Generic medicines are less effective than brand-name medicines	5	4	3	2	1
i	Generic medicines produce more side effects than brand-name medicines	5	4	3	2	1
j	Generic medicines are less expensive than brand-name medicines	5	4	3	2	1
k	Brand-name medicines must meet higher safety standards than generic medicines	5	4	3	2	1
l	I need more information on the issues pertaining to the safety and efficacy of generic medicines	5	4	3	2	1
m	I find it easier to recall a medicine's therapeutic class using generic names rather than brand names	5	4	3	2	1
n	In the medical insurance system, I have received lectures and practical training about the burden of medical expenses between the self-pay and public insurance system	5	4	3	2	1

Fig.1 The questionnaire used in this study

The questionnaire comprised seven sections to elucidate pharmacy students' knowledge and perceptions of generic medicine. The seven sections included questions evaluating gender (Q1); year of study (Q2); age (Q3); educational background before admission in the faculty of pharmaceutical sciences (Q4); knowledge of bioequivalence (Q5); the tolerance range at a 90% confidence interval of the mean blood concentration ratio of generic medicines and brand-name medicines in bioequivalence studies (Q6); and knowledge of the difference between

generic and brand-name medicines and perceptions of education on generic medicines (Q7a-n). These seven questions were developed based on the questionnaire used by Hassali et al [8]. This study was approved by the research ethics committee of Graduate School of Pharmaceutical Sciences, Chiba University.

2. Comparison the knowledge and perceptions of generic medicines by year

We compared responses to Q5 (knowledge of bioequivalence) and Q6 (tolerance range at a 90% confidence interval for mean blood concentration ratio of generic medicines and brand-name medicines in bioequivalence studies) by the participant year groups. We also compared mean scores for Q7 (knowledge of the difference between medicine types and perceptions of education of generic medicines) using a 5-point Likert scale (1 = Strongly disagree, 2 = Disagree, 3 = Neutral, 4 = Agree, and 5 = Strongly agree) and between the 3rd year and 4–6th year students.

3. Statistical analyses

We evaluated the proportions of each gender and educational background using the chi-square test. Knowledge of the differences between generic medicines and brand-name medicines, as well as education of generic medicines, were assessed using the *Kruskal-Wallis* H-test. Significant differences were followed up with pair-wise comparisons using the Steel test for multiple comparisons. A nominal alpha of 0.05 was used for statistical tests. All statistical analyses were performed using SPSS Statistics 25.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 626 students completed the questionnaire (response rate of 98.6%), including 150 in 3rd year, 162 in 4th year, 162 in 5th year, and 152 in 6th year. There were no significant differences in the proportions of each gender and educational background by year of study.

The results for Q5 and Q6 are shown in Figure 2. Regarding Q5, the percentage of respondents who answered "I understand the meaning of bioequivalence" was highest among 5th year students (67.3%), followed by 6th year (58.6%), 4th year (31.5%), and 3rd year (14.0%) students. As for Q6, the proportion of choosing the correct answer of "80–125%" was less than 5% regardless of year, which was extremely low.

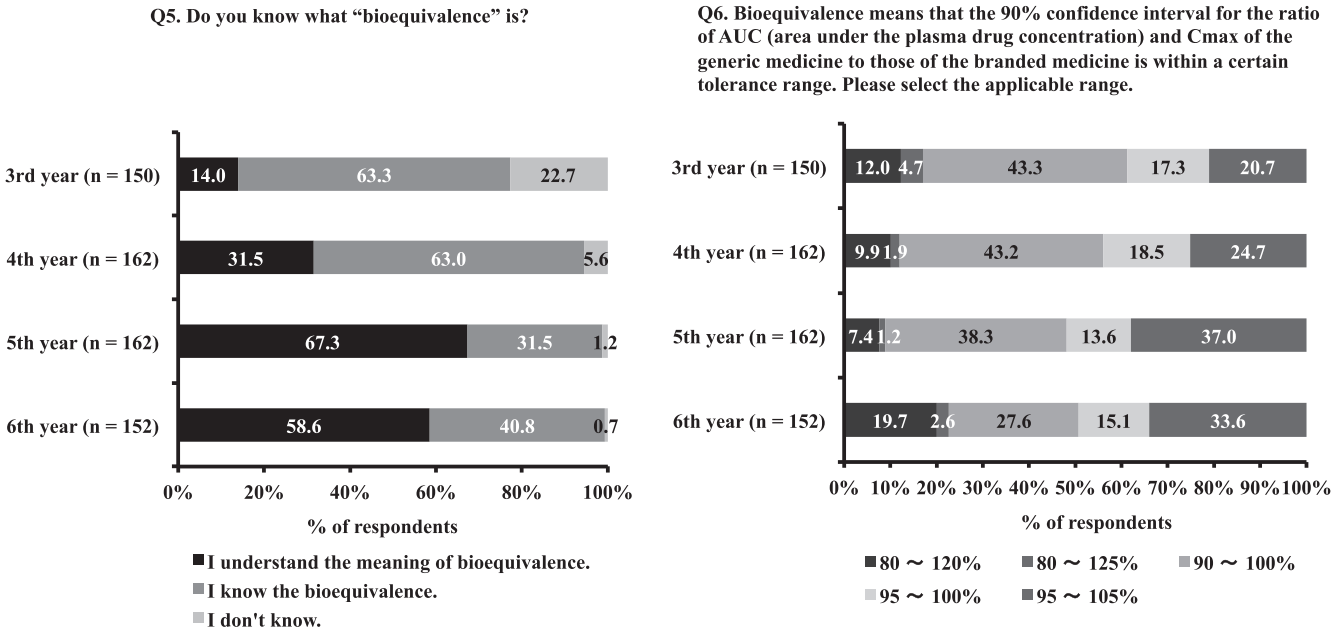

Fig. 2 Recognition of bioequivalence

Table 1 displays the results for Q7a–Q7d, which ask about knowledge and perceptions about generic equivalence. Responses to questions 7a and 7d did not significantly differ by year of study. However, for Q7b, the mean ratings of 5th and 6th year students significantly differed from those of 3rd year students—that is, senior students were more likely to "disagree" or "strongly disagree" that generic medicines are therapeutically equivalent to each other (P < 0.01). Furthermore, 4th to 6th year students were significantly more likely to "agree" or "strongly agree" that they had been introduced to the issues of bioequivalence for generic medicines (Q7c) compared to 3rd year students (P < 0.01).

Table 1 Knowledge and perceptions about generic equivalence

	Q7	3rd year (n = 150)	4th year (n = 162)	5th year (n = 162)	6th year (n = 152)	*P-value*[a)]	*P-value*[b)]		
							3 – 4 year	3 – 5 year	3 – 6 year
a	All generic products of a particular medicine rated as generic equivalents are therapeutically equivalent to the brand-name medicine	3.6±0.8	3.7±0.9	3.7±0.9	3.5±1.0	0.10			
b	All generic products of a particular medicine rated as generic equivalents are therapeutically equivalent to each other	3.1±0.9	3.0±1.1	2.7±1.0	2.7±1.0	< 0.01	0.97	< 0.01	< 0.01
c	I have been introduced to issues on the bioequivalence of generic medicines during my pharmacy education	2.9±1.0	3.8±1.1	4.1±0.8	3.8±0.9	< 0.01	< 0.01	< 0.01	< 0.01
d	I need more information on how bioequivalence studies are conducted for generic medicines	3.5±0.7	3.7±0.7	3.6±0.7	3.4±0.8	0.14			

Mean ± S.D. a) Kruskal-Wallis test b) Steel test

Table 2 shows the results for Q7e–Q7k, which concern perceptions of the dosage form, dose, quality, efficacy, side effects, prices, and safety of generic versus brand-name medicines. Post hoc pair-wise comparisons indicated that, compared to students in 3rd year, students in 5th and 6th year were significantly more likely to agree that generic medicines must contain the same dose as brand-name medicines (P < 0.01). In addition, compared to 3rd year students, 4th and 5th year students were significantly more likely to "disagree" or "strongly disagree" that generic medicines are of inferior quality, less effective, and produce more side effects than brand-name medicines (P < 0.01). Students in the 4th to 6th years were also significantly more likely to "agree" or "strongly agree" that generic medicines are less expensive than are brand-name medicines compared to 3rd year students (P < 0.01). Responses to Q7e and Q7k did not significantly differ by year of study.

Table 2 Perceptions of the dosage form, dose, quality, efficacy, side effects, drug prices, and safety of generic medicines versus brand-name medicines

	Q7	3rd year (n = 150)	4th year (n = 162)	5th year (n = 162)	6th year (n = 152)	*P-value*[a)]	*P-value*[b)]		
							3 – 4 year	3 – 5 year	3 – 6 year
e	A generic medicine must be in the same dosage form (e.g., tablet, capsule) as the brand-name medicine	2.3±0.9	2.3±1.1	2.5±1.2	2.2±1.1	0.06			
f	A generic medicine must contain the same dose as the brand-name medicine	2.8±1.0	3.0±1.3	3.6±1.2	3.6±1.2	< 0.01	0.42	< 0.01	< 0.01
g	Generic medicines are inferior in quality than brand-name medicines	2.3±0.8	2.0±0.9	1.9±0.7	2.2±0.9	< 0.01	< 0.01	< 0.01	0.66
h	Generic medicines are less effective than brand-name medicines	2.4±0.8	2.0±0.9	1.8±0.7	2.2±0.8	< 0.01	< 0.01	< 0.01	0.22
i	Generic medicines produce more side effects than brand-name medicines	2.3±0.7	2.1±0.9	2.0±0.7	2.2±0.8	< 0.01	< 0.05	< 0.01	0.17
j	Generic medicines are less expensive than brand-name medicines	4.1±0.7	4.5±0.8	4.5±0.6	4.5±0.6	< 0.01	< 0.01	< 0.01	< 0.01
k	Brand-name medicines must meet higher safety standards than generic medicines	3.1±1.0	3.1±1.1	3.0±1.1	3.1±1.0	0.50			

Mean ± S.D. a) Kruskal-Wallis test b) Steel test

Table 3 shows responses to Q7l–Q7n, which concern perceptions about current pharmacy education on generic medicines. We found that perceptions regarding the need for more information on the safety and efficacy of generic medicines did not vary by year of study. However, compared to students in 3rd year, students in 5th and 6th year reported a significantly greater tendency to find it easier to recall a therapeutic class of a drug using generic names rather than brand-name medicines (P < 0.01). Furthermore, students in 4th to 6th years were more likely to "agree" or "strongly agree" that they had received lectures and practical training about the burden of medical expenses between the self-pay and public insurance system compared to 3rd year students (P < 0.01).

Table 3　Perceptions of current pharmacy education about generic medicines

	Q7	3rd year (n = 150)	4th year (n = 162)	5th year (n = 162)	6th year (n = 152)	*P-value*[a)]	*P-value*[b)]		
							3 – 4 year	3 – 5 year	3 – 6 year
l	I need more information on the issues pertaining to the safety and efficacy of generic medicines	3.6±0.7	3.8±0.7	3.6±0.8	3.5±0.8	0.06			
m	I find it easier to recall a medicine's therapeutic class using generic names rather than brand names	3.6±0.9	3.7±0.8	4.0±0.9	4.2±0.9	< 0.01	0.60	< 0.01	< 0.01
n	In the medical insurance system, I have received lectures and practical training about the burden of medical expenses between the self-pay and public insurance system	3.1±1.0	3.5±1.0	4.1±0.7	4.0±0.7	< 0.01	< 0.01	< 0.01	< 0.01

Mean ± S.D.　a) Kruskal-Wallis test　b) Steel test

Discussion

This study examined the knowledge and perceptions of generic medicine in 3rd to 6th year students of the Faculty of Pharmaceutical Sciences. There was an overall lack of knowledge among participants, irrespective of the year of study. In particular, the results of Q5 and Q6 indicated that students did not have sufficient knowledge of bioequivalence studies of generic medicines. Knowledge of bioequivalence is essential for interpreting the results of such studies, and the findings of this study indicate that education on bioequivalence should be introduced earlier and covered more comprehensively in pharmaceutical science education. Indeed, being able to evaluate the bioequivalence of different formulations of prescription medicine (e.g., brand-name and generic medicine, changes in pharmaceutical formulations during development) is one of the specific behavioral objectives (SBO) of the Model Core Curriculum for Pharmaceutical Education (2015 version)[9]. A previous questionnaire survey of pharmacy students receiving practical training on generic medicine (focusing on conveying understanding of its characteristics and roles) showed that the degree of comprehension of bioequivalence is related to students' subjective understanding of generic medicine[10]. Accordingly, students should be educated on how to interpret tolerance in bioequivalence studies for generic medicines[11] in order to obtain a proper understanding of generic medicines. Properly trained students will, in the future, be able to contribute to proper promotion of the use of generic medicine.

Regarding the results of the comparison between 3rd and 4th to 6th year students' knowledge and perceptions of generic equivalence, the latter group had a significantly better understanding than did the former of Q7b, but there was no significant difference in Q7a (i.e., knowledge of the basic definition of generic medicine). These results provide further evidence of the need to strengthen education. As for Q7c, 4th to 6th years were both significantly more likely to answer "agree/strongly agree" than were 3rd year students, but there was no significant difference between the groups in Q7d. These results suggest a gap: while students mentioned having a degree of knowledge of bioequivalence, their reported understanding of it was insufficient. Most participants had only received education on bioequivalence of generic medicines

in the form of lectures. It is therefore necessary to improve the educational curriculum to ensure that students obtain a greater understanding of bioequivalence, such as by incorporating new exercises to confirm the equivalence of pharmacokinetics between generic and brand-name medicines.

In the comparison of knowledge of the dosage form, dose, quality, efficacy, side effects, drug prices, and safety of generic medicine, the mean scores increased significantly with year of study for Q7f and Q7j. This suggests that they gained sufficient understanding of the definition of generic medicine and the economic effect of promoting its use. On the other hand, although knowledge increased in the 4th and 5th years for Q7g, Q7h, and Q7i, there was no significant difference for the 6th year students. One possible reason for this result is that during the practical training at hospitals and pharmacies conducted in the 5th year, participants might have encountered cases where there were evident differences in the quality, efficacy, and safety of generic medicines compared with brand-name medicines. Some previous studies have found that the effectiveness and quality of certain generic medicines are inferior to those of their brand-name counterparts[4-6]. On the other hand, the Ministry of Health, Labour and Welfare regularly issues "generic medicine quality information" which provides evidence of the quality of generic medicines. Although the results of this survey indicate that students generally have sufficient knowledge of the quality, efficacy, and side effects of generic medicines, it seems necessary to continue to educate them on this topic through lectures and practical training to ensure further promotion of the use of generic medicines.

Our results also indicate that students found it easier to recall a medicine's therapeutic class using generic rather than brand-names as they progressed through their education. Unlike pharmacists in the clinical setting, students recognized the names of medicines through their generic names rather than their brand-names. To promote the prescription of generic name medicines, the Japanese government has made it possible for pharmacists to switch generic medicine and has allowed patients to request generic medicines at the pharmacist's discretion. For these reasons, education on generic prescriptions remains necessary.

The SBO on generic medicines explicitly listed in the Model Core Curriculum for Pharmaceutical Education (2015 version) states that "the student is able to evaluate the bioequivalence of different formulations of prescription medicine (e.g., brand-name and generic medicine, changes in pharmaceutical formulations during development)" and "it is possible to compare and evaluate the quality, safety, economic efficiency, etc. of the brand-name and the generic medicine based on the drug information." Also, the outcomes of practical training are usually evaluated using rubrics, which ensures that pharmacists and students can effectively learn while sharing goals[12], and students are expected to be able to deepen their understanding of the SBO. Therefore, education of generic medicines is considered more substantial.

Based on the above findings, we might suggest an ideal future curriculum for education on generic medicines. First, early on in the course, lectures on the benefits of promoting the use of generic medicines from the viewpoint of pharmaceutical development and medical economics should be held. By fourth year, when students begin preparing for practical training, exercises could focus on providing students with more detailed knowledge of the adoption and selection of generic medicines. This curriculum will produce pharmacists who can contribute to promoting appropriate use of generic medicines.

Overall, the results of this study suggest that pharmacy students lack knowledge of bioequivalence. By enriching knowledge of the evaluation of bioequivalence studies of generic medicines in undergraduate education, students will be better equipped to promote the use of generic medicines. Although the current findings are compelling and important, the data were obtained from a small sample of pharmacy students at two facilities. Thus, the current results may not be generalizable to other pharmacy students. It is therefore important that

future studies recruit larger sample sizes with varying demographic characteristics and students from other pharmaceutical training programs. In addition, it is also necessary to investigate not only pharmacy students but also medical students, and utilize these results for future education on generic medicines.

Conflicts of interest: COI

The authors declare no conflicts of interest.

References

1）Ministry of Health, Labour and Welfare: Market share of generic medicine. http://www.mhlw.go.jp/file/06-Seisakujouhou-10800000-Iseikyoku/0000114512.pdf access 2018-04-10.

2）Ministry of Health, Labour and Welfare: basic policy 2015 of the economic financial administration and reform. http://www.mhlw.go.jp/file/05-Shingikai-12404000-Hokenkyoku-Iryouka/0000090891.pdf access 2018-04-10.

3）Ministry of Health, Labour and Welfare: a road map for further use promotion of the generic medicine. http://www.mhlw.go.jp/stf/houdou/2r9852000002z7fr-att/2r9852000002z7it.pdf access 2018-04-10.

4）Eichi S, kei K: A case of palpitation caused by an increase in heart rate due to change to generic product. J. New Rem. & Clin., 57(3), 367-370, 2008.

5）Kashima A, Yabuki H, Morohashi A, Fukumoto K, Ueno K: Quality Evaluation of Original and Generic Products of Theophylline Sustained-release Dry-syrup Preparations. Jpn. J. Pharm. Health Care Sci., 32(11), 1088-1093, 2006.

6）Ishizaka T, Okada S, Tokuyama E, Mukai J, Uchida T: Quality of twelve clarithromycin dry syrup formulations-bitterness, grittiness and uniformity of drug loading. Chem. Pharm. Bull., 56(10), 1389-1394, 2008.

7）Ministry of Health, Labour and Welfare: Information on the quality of generic medicines. http//www.mhlw.go.jp/stf/seisakunitsuite/bunya/kenkou_iryou/iyakuhin/kouhatsu_iyakuhin/index.html, access 2018-08-3.

8）Hassali MA, Kong DC, Stewart K: A comparison between senior medical students' and pharmacy pre-registrants' knowledge and perceptions of generic medicines. Med Educ., 41(7), 703-710, 2007.

9）Ministry of Education, Culture, Sports, Science and Technology: Model Core Curriculum for Pharmaceutical Education - 2015 version -, http://www.mext.go.jp/b_menu/shingi/chousa/koutou/058/gijiroku/__icsFiles/afieldfile/2014/11/10/1352956_2.pdf access 2018-01-4.

10）Erisa T, Akio K, Tomoaki H, Junichiro S, Keiko N, Toshiro M: Training Program on Generic Drugs at a Pharmacy School and its Effects. Jpn J Pharm Health Care Sci., 39(10), 624-634, 2013.

11）Ministry of Health, Labour and Welfare: Guideline for Bioequivalence Studies of Generic Products, Notification No.10, adopted February 2012. http://www.nihs.go.jp/drug/be-guide(e)/Generic/GL-E_120229_BE.pdf access 2018-04-10.

12）Yasuhara M, Sone T, Kohno T, Ogita K. Concept Extraction of Graduate Research by Modified Grounded Theory Approach and Creating of Rubric Oriented to Performance Evaluation. YAKUGAKU ZASSHI. 2015; 135. 99-105.