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RESEARCH ARTICLE

Fostering critical thinking in pharmaceutical chemistry: A cross-sectional study

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Abstract

Background: The fundamentals of pharmaceutical chemistry are difficult to relate to the pharmacy profession for first-year pharmacy students, and most of them use the surface approach to complete it. This study aimed to determine pharmacy students' perception and critical thinking skills in solving real problem-based questions. **Methods:** This study employed pre- and post-survey to understand undergraduates' perceptions and critical thinking skills in solving questions through a problem-based approach. **Results:** A total of 130 respondents (74%) participated in the questionnaire survey. After completing problem-based questions, pharmacy students were able to apply basic organic concepts to solve questions on synthesis pathways and impurities and relate to regulatory and environmental, social, and governance guidelines. The majority of pharmacy students highly rated the collaborative problem-based learning session and found the questions relevant to the pharmacy profession. **Conclusion:** In conclusion, carefully designed problem-based assignment questions could train pharmacy students with twenty-first-century skills.

Introduction

The twenty-first-century online learning outlines a framework for heuristic evaluation, encompassing critical thinking, problem-solving, and creativity skills (Nacu, Martin & Pinkard, 2018). First-year pharmacy students entering public universities in Malaysia were educated through the formal didactic formative teaching and learning education system. Most pharmaceutical organic chemistry courses were taught according to the traditional teaching and learning practices, where lectures cover topics from organic chemistry books every week for fourteen weeks each term (Choo & Abdul Rahim, 2021). The evaluation was based on both summative and formative assessments. The summative assessments included laboratory practical or tutorial-based assignments. The coronavirus disease in 2019 (COVID-19) has disrupted face-to-face teaching and learning activities, which were switched to online

distance learning. The internet was truly the saviour during the pandemic lockdown. It allowed online education, regardless of the distance or whereabouts of all enrolled students. The internet also allowed students to access limitless or borderless information from various online sources in video or written article format. Answers to textbook-based questions, especially those related to Bloom's taxonomy on the remembering and understanding cognitive domain, were readily available through "googling" or searching relevant keywords in internet search engines. Thus, lecturers need to rethink their identity and reflect on their role in teaching and that of students in learning (Sullivan, 2021). Online learning opens another dimension of learning beyond those didactic traditional teaching methods representing the students' future working lifestyle. Indirectly, the pandemic has expedited the implementation of twenty-first-century skills into online learning.

The twenty-first-century skills were highlighted by a few countries and international organisations, such as the Asia-Pacific Economic Corporation (APEC) and the Organisation for Economic Co-operation & Development (OECD), in the early 1980s and were not limited to knowledge-based content. A study has grouped these skills into three main areas: learning and innovation skills (include critical thinking and problem-solving, collaboration and communications, creativity, and innovation), digital skills (encompass information literacy, media literacy, information, and communication technologies), and life skills (adaptability, self-direction, social interaction, productivity, and accountability) (Joynes, Rossignoli & Amonoo-Kuofi, 2019). Recognising these required skills, the education system needs to shift from the traditional content-based method to the inclusion of higher-order thinking skills or deeper learning. This pedagogy involves creating, working with others, analysing, presenting, and sharing both learning experiences and learned knowledge or wisdom between peers and facilitators. In addition to content-based pedagogies, active, project-based, and problem-based learning, as well as other methods, should be included in new curricula to promote in-depth knowledge.

The problem-based learning (PBL) approach is an instructional method that guides students in solving real-world problems (Savery & Duffy, 1995). PBL questions are not well structured to encourage interactions to help solve problems (Gao *et al.,* 2018). It has been reported that the implementation of PBL with more than one group at the same time is difficult to control (Albanese & Mitchell, 1993) as it is difficult to organise information from different groups. Further, inquiry-guided learning (IBL) is a problem- or question-driven approach that integrates inquiry in a student-led activity. Both approaches, IBL and PBL, are quite similar since learning occurs when learners are actively engaged in the process of developing an understanding of a problem (Carriger, 2015). Active student engagement alone in PBL cannot only be stimulated by a practice-relevant problem. According to IBL, it can also be nurtured by an academic issue that places students in a situation where they are engaged in inquiry in a group (Lazonder & Harmsen, 2016). Thus, the integrated approach of inquiry-guided problem-based learning was used for this study since this is the student's first exposure to this active learning approach.

Critical thinking is a subset of the three thinking processes of reasoning, making judgments and decisions, and problem-solving (Willingham, 2008). Content knowledge is needed to achieve appropriate critical thinking in the knowledge domains. Through critical thinking, students focus on the processes of learning rather than just attaining facts about a phenomena (Rubenfeld & Scheffer, 2006). Critical thinking helps learners gain and apply new knowledge to real-world situations. When learners think critically, they become actively responsible for their education, thus leading to wisdom and not merely learning new information (Walker, 2005).

This research aims to understand the student's perception of solving problem-based questions requiring critical thinking while integrating the content of fundamental pharmaceutical chemistry and real practice-related situations.

Methods

Description

The design of the inquiry-guided problem-based assignment needs careful consideration. Understanding chemistry reactions has been a student dilemma (Rodemer et al., 2021); thus, a pre-survey was conducted to understand student knowledge of these topics. The instructional design of the repeating topics can be expanded to cover more in-depth learning inclusive of both the United Nations sustainable development goals (SDGs) and regulatory topics related to their profession. Students had to explain which synthesis route uses the minimal amount of chemicals and produces lesser impurities and provide reasons for fulfilling any of the seventeen SDGs criteria. This could help the students integrate the basic organic chemistry knowledge into their decision-making, governed by global regulatory and sustainability compliance. An evidence-based approach was used for the design of the problem-based assignment by gathering information from students. Research evidence and local evidence from students were used for the course design (Hrastinski, 2021).

Fundamentals of pharmaceutical chemistry is a first-term course for undergraduate pharmacy students, where they experience virtual mass lectures and virtual problem-based assignments for the first time. Google Classroom (GC) was utilised as the learning management system (LMS). The live stream briefing session and problem-based questions were posted a week earlier. The class of 176 students was divided into groups of five members each. Each facilitator handled 5-6 groups. Due to the intermittent disruptions of internet connectivity, both asynchronous and synchronous communications were used for the discussion. The facilitator's function was to guide the students on the right track toward completing the task. Each team had to present the findings in a fixed-size digital poster (e-Poster).

Content of the inquiry-guided problem-based assignment

The inquiry-guided problem-based questions were linked, and it covered four topics from the course content. Since pharmacy students were exposed for the first time to problem-based type of questions, simple instructions or inquiries were created with the problem-based question to guide them in solving the problems. A hypothetical alkyl halide and nucleophile was designed for the synthesis of the enantiomer pure (R)-ibuprofen. Pharmacy students were provided with the following: i) a monograph of (RS)-ibuprofen from the British pharmacopoeia, ii) an article related to (S)+ibuprofen pharmacology, and iii) International Council for Harmonisation (ICH) Guidelines on Q3A(R2) impurities in new drug substances. In these PBL sessions, students learned how to identify i) physical and chemical properties extracted from the pharmacopoeia to differentiate the (RS) enantiomers from the enantiomer pure (R) or (S)-ibuprofen, ii) the synthesis route following either the unimolecular or bimolecular elimination or substitution pathway, iii) the side products or impurities and the pharmacology of racemate mixtures or enantiomer pure active pharmaceutical ingredient (API), and iv) the effect of the choice of synthesis route on the sustainable development goals (SDGs).

The PBL question is as listed below.

After graduation, you are employed as an intern in a pharmaceutical company that has pledged to the 2030 deadline of Sustainable Development Goals (SDGs) set by the United Nations. As a young intern in the pharmaceutical company, you are assigned to propose the development of a new pharmaceutical consisting of enantiomeric pure (S)+ibuprofen. The head of the product development department provided you with information consisting of 1) a monograph of (RS) ibuprofen from the British Pharmacopoeia 2011, 2) an article related to the pharmacology of (S)+ibuprofen and 3)ICH Q3A (R2) Impurities in New Drug Substances.

To work with the formulation team, you need to get the active pharmaceutical ingredient (API) product specification from the suppliers. Decide what are the main chemical and physical characteristics of the API you need to acquire from the suppliers

With regard to the ICH Q3A on the Impurities in New Drug Substances guideline, identify the plausible impurities of the (S)+ibuprofen. The API manufacturer informed that the (S)+ibuprofen was synthesized using (CH3)2CHCH2PhCH(CH3)(Br) and ethyne. With your knowledge of Substitution or Elimination reactions of alkyl halides, propose the route of synthesis and its plausible impurities. Discuss whether this route of synthesis conforms to your company's SDG initiatives.

Questionnaire development and validation

The questionnaire used in this research project was adapted from an unpublished report that had it pilot-tested and could demonstrate good face and content validity. The face validity that involved assessing the readability, length, and relevance of the online questionnaire was done by three senior pharmacy lecturers who had been trained in questionnaire design. Pre-testing was also conducted, where 38 students were involved. The internal consistency of the final questionnaire was determined using Cronbach's alpha coefficient (Cronbach's alpha value was 0.78).

All students were subjected to a pre- and post-survey to assess their understanding of the topics, exposure to pharmacopoeia, impurities regulation, and SDG goals. The post-survey included demographic features and the problem-based questions' level of difficulty. The study was approved by the KPJ Healthcare University College Research Ethics Committee (Reference number: KPJUC/RMC/SOP/EC/2022/387).

Data analysis

A 5-point Likert scale was used to measure students' perception of questions' difficulty level. It was rated as strongly agree (4.21-5.00), agree (3.41-4.20), neutral (2.61-3.40), disagree (0.81-2.60), and strongly disagree (0-0.80). The descriptive mean, mean score and standard deviation were calculated using Microsoft Excel (version 2107). Reliability coefficients greater than 0.70 are generally acceptable, values greater than 0.80 are adequate, and values greater than 0.90 are good (Nunnally & Bernstein, 1994).

Results

Pre-survey results

Out of a total of 176 students, 130 pharmacy students (74%) enrolled in the Bachelor of Pharmacy course, responded to the questionnaire survey, with 19% male and 81% female. All Bachelor of Pharmacy students have a minimum CGPA of 3.50 from pre-university programmes, i.e. Foundation, Matriculation Programmes, or Pharmacy Diploma, with a minimum of two years of working experience. The pre-survey showed that more than 70% of first-year pharmacy students had learned topics related to alkyl halides, substitution, and elimination reactions during pre-university. Other topics, such as enantiomer, pure enantiomer, impurities, monographs, ICH guidelines, and SDGs, were new to most of them (Figure 1).
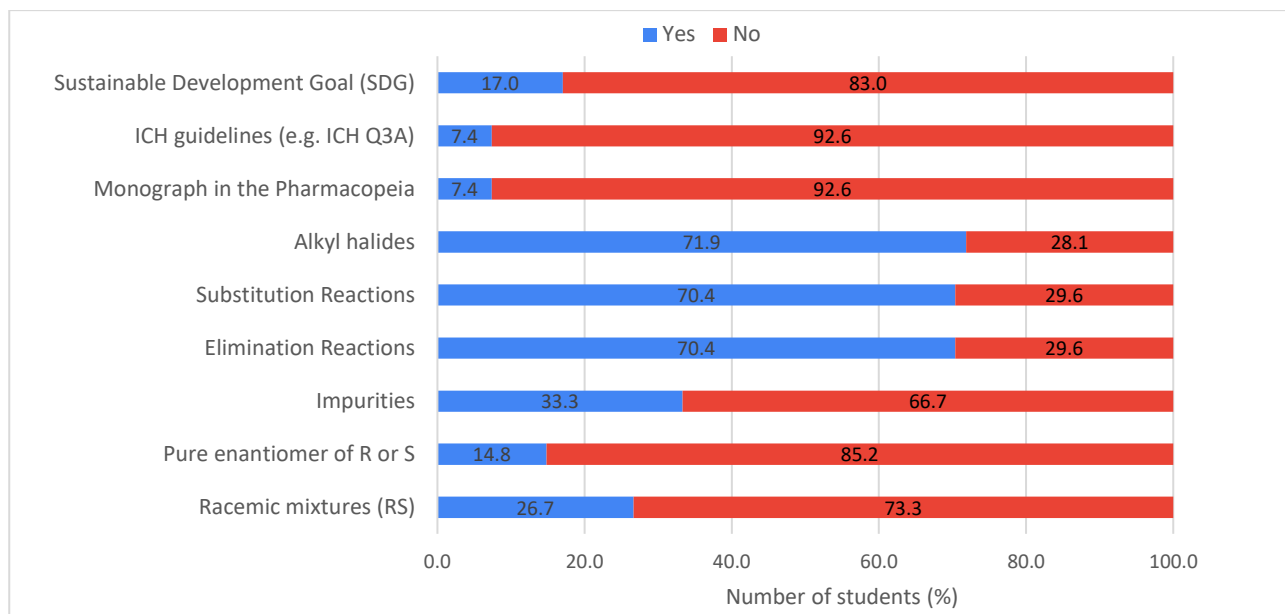
Figure 1: Pre-survey responses on pharmacy students' prior learning experience

Students' perception of the inquiry-guided problem-based questions

The students rated questions 1-4 as difficult (Table I). These were application questions requiring the process of reasoning, making judgments, and problem-solving, such as finding the physical and chemical properties in the pharmacopoeia to solve the questions, identifying elimination or substitution reaction to produce an enantiomer pure (R)-ibuprofen, and understanding the ICH guidelines to classify impurities from the synthesis. The remaining questions were neither difficult nor easy.

Table I: Student's perception of the level of difficulty in problem-solving

No.	Rate the level of difficulty to solve problems related to these questions	Mean	Standard deviation
1	I find it easy to identify the physicochemical properties from the monograph in the pharmacopeia to solve the question	3.8	0.9
2	I find it easy to identify either elimination or substitution reactions to produce (*R*)-ibuprofen	3.8	0.8
3	I find it easy to understand the global guidelines (e.g., ICH Q3A) governing the content of pharmaceutical impurities	3.8	0.9
4	I find it easy to identify the pharmaceutical impurities from the production of (*R*)-ibuprofen	3.6	0.9
5	I find it easy to identify the SDG goals related to the choice of reactions (enantioselective reactions)	3.3	1.0
6	I find it easy to differentiate the pharmacological properties of racemic mixtures from enantiomer pure ibuprofen	3.2	0.8
7	I find it easy to differentiate between racemic mixture from enantiomer pure ibuprofen	3.0	0.9
8	I find it easy to identify the physical and chemical properties of racemic mixtures and enantiomer pure ibuprofen	2.9	0.8

After completing the PBL assignment, students agreed (3.41-4.20) that they understand the application of fundamental organic chemistry knowledge in the pharmaceutical industry, the definition of impurities, and the influence of SDG in decision-making. They also agreed that they know how to identify the type of reactions and impurities and extract physicochemical characteristics from the pharmacopoeia (Table II). This result indicates that the questions helped them better understand this topic.

Table II: Student's level of understanding after PBL assignment

No.	Description	Mean	Standard deviation
1	I understand the application of basic organic chemistry in the pharmaceutical industry	3.73	0.07
2	I understand how to identify either elimination or substitution reaction from the starting material	3.77	0.08
3	I understand how to identify the impurities produced in an elimination or substitution reaction	3.68	0.08
4	I understand the effect of impurities in pharmaceuticals	3.85	0.07
5	I understand how to extract information in the monograph from the pharmacopeia	3.75	0.08
6	I understand the definition of impurities as specified by Global guidelines e.g., ICH Q3A	3.73	0.07
7	I understand the influence of SDG in decision making	3.91	0.07

Discussion

Although the pre-survey showed that more than 70% of participants had studied the substitution and elimination reaction during pre-university, students found it hard to apply their knowledge in real-world situations to a small-size drug molecule, i.e., ibuprofen, as indicated in their responses in question no. 2 (Table I).

The surface approach (including memorising and reproducing the learning material) was easily applied by students (Lindblom-Ylänne, Parpala & Postareff, 2019), whereas promoting the in-depth learning approach seems to be more problematic (Marton & Säljö, 1997). Students had previously completed two hours of didactic traditional instructional lecture on stereoisomerism. Yet, they found question no.7 (Table I) difficult on the method to differentiate racemic mixtures from single enantiomer pure ibuprofen. This result confirmed the surface approach that most students applied when studying fundamental organic chemistry. Finally, by incorporating concept questions to solve real-world problems, pharmacy students could reflect on the taught content, critically evaluate the information learned, and apply the concept to a small-size drug structure.

Two questions related to extracting the relevant information from the pharmacopoeia (no.1) and identifying relevant information from ICH guidelines on pharmaceutical impurities (no.3) in Table I were rated as difficult by the students. Content knowledge is needed to achieve appropriate critical thinking in knowledge domains. As mentioned in a previous study, it takes grit to continue with PBL to foster the twenty-first-century critical thinking skill required by employers (Nussbaum *et al.,* 2021).

Students' opinions regarding the PBL

Overall, 85.7% of students enjoyed the PBL session. Upon course completion, students rated the teaching and learning activities as excellent (91%) using the university's online feedback form. It is recommended to introduce well-designed problem-based questions to first-year pharmacy students as two of the organic synthesis modules, namely fundamentals of pharmaceutical chemistry and pharmaceutical organic chemistry, are completed during this study year. Exposure to real-world problems allowed participants to connect to their profession.

Limitations

First-term pharmacy students found it hard to apply the theoretical concepts learned during lectures to real-world problems. Hence, PBL was modified to inquiry-guided PBL sessions to lessen their stress. As they progressed to the second term, the design of PBL included having to uncover the issue of a problem by themselves. The initial implementation of PBL was challenging, as pharmacy students found it hard to adapt. After explaining why PBL was introduced, they were able to adapt to the new learning method. This study did not evaluate the improvement of students' critical thinking abilities throughout their four years of study.

Extrinsic motivation, such as extra marks, should be considered in the future to increase student participation in discussions. Although pharmaceutical chemistry is the core subject in pharmacy courses, students complete their fundamentals of pharmaceutical chemistry related to stereoisomerism, synthesis, and organic chemistry during their first year. Thus, the introduction of API monographs from the pharmacopoeia was taught at an early stage to expose first-year students to the physicochemical properties and analytical information of drugs and merge with industrial practice. Finally, students appreciated the feedback provided to them regarding the assignment.

Conclusion

This study generated novel findings about pharmacy students' perceptions and critical thinking skills in solving real-world problem-based questions. More than three-quarters of the participants reported having enjoyed the PBL session and rated this teaching and learning activity above 90%. The findings indicated that first-year pharmacy students adjusted to an inquiry-guided problem-based approach to learning the fundamentals of the pharmaceutical chemistry course. A carefully developed instructional designed problem-based assignment questions could train pharmacy students with twenty-first-century skills, namely critical thinking, problem-solving, collaboration, digital literacy, and life skills to solve real-world problems.

Conflict of interest

The authors declare no conflict of interest.

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