RESEARCH ARTICLES

A Quantitative Assessment of a Medicinal Chemistry Problem-based Learning Sequence

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Objectives. To establish an aggressive problem-based learning (PBL) format for the medicinal chemistry course and assess the outcomes of student learning.
Methods. To assess learning in the new format, precourse and postcourse examinations were given to students enrolled before and after problem-based learning was implemented, and appropriate statistical analyses were conducted.
Results. The PBL cohort did not learn the same amount of factual content yet performed the same on higher-order thought questions as the non-PBL cohort.
Conclusions. Problem-based learning may not be the ideal method for teaching medicinal chemistry. This may be due to several factors including: student learning type, the lack of a cognitive framework for learning in the basic sciences, and time constraints.
Keywords: problem-based learning, medicinal chemistry, assessment

INTRODUCTION

Problem-based learning (PBL) was first implemented in a medical education curriculum by Toronto's McMaster University in the late 1960s. Numerous definitions of problem-based learning abound. Both Albanese and Anderson-Harper provide excellent reviews of PBL and PBL in pharmacy education respectively.[1,2]

Over the last several years, the McWhorter School of Pharmacy has pursued a concerted course of action to implement active learning and problem-based learning strategies across the doctor of pharmacy curriculum. As part of The Pew Charitable Trusts funded initiative in PBL at Samford University, 13 core curriculum courses, covering all or part of 54 course credits and representing 48% of the pharmacy curriculum's didactic offerings, were redesigned into a PBL format and delivered as such. Beyond the Pew supported initiatives, several additional core and elective courses were developed and delivered in a PBL-like format. The 2-semester medicinal chemistry sequence was part of this redesign initiative.

Over the 5 years leading up to the PBL initiative, the instructors incorporated increasing amounts of active learning within the course sequence. The out-of-class problems required the application of the concepts central to medicinal chemistry in the design of novel drug molecules. These exercises increased to 5 group exercises per semester in the year prior to the intentional restructuring of the course sequence. The main purpose had been to reinforce existing course content rather than create portals for new learning.

The pharmacy education literature is replete with examples of case-based teaching. Currie et al used patient case studies in a medicinal chemistry course.[3] The cases were developed and jointly facilitated with pharmacotherapeutics faculty members. The students worked in groups and were quizzed at the end of the group session. The authors cite evidence that the students learned medicinal chemistry better with this approach. No quantitative assessment of examination scores was given. Alsharif et al developed a rubric as a means of teaching medicinal chemistry in a case-based manner.[4] The rubric facilitated the students' approach to the problem. The rubric was used to solve problems on homework assignments and on examinations. A critique of this particular rubric is twofold: pharmacotherapeutics is emphasized over medicinal chemistry and elements of the rubric can not be addressed by the consideration of the drug structures in question. The closest example to the approach we used is that of Herrier et al who used groups to work through cases to teach pharmacology and medicinal chemistry.[5] The courses were separate didactic courses. Lectures

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were used at the beginning of the course for introductory purposes. The authors concluded that there was an improvement in knowledge of pharmacology but no real improvement was seen in medicinal chemistry knowledge. Overall the students felt that the course improved their self-learning skills. In summary, the use of case studies in teaching medicinal chemistry has merit in encouraging students to apply their knowledge, thus reinforcing learning. Our goal was to enhance learning of medicinal chemistry content and principles that can be applied to solving pharmacotherapeutic issues in the therapeutics courses and in practice.

Our central premise in the design of the new syllabus was to incorporate group resolution of problems in the classroom to provide a foundation for learning. This is a significantly different approach than previously employed. To this end we designed new problems along with utilizing resources already in print, especially the *Medicinal Chemistry Case Study Workbook*.[6] Student groups were required to maintain a course portfolio each semester which included copies of their group problems and presentations, along with peer and self-assessments.

METHODS

Because the actual conversion to an active-learning format did not take place until the final year of the Pew grant, we were able to perform a pre/post comparative evaluation between a non-PBL cohort and the first PBL cohort. The demographics of both cohorts were similar. The non-PBL cohort (N = 102) was 78% female, 84% Caucasian, with an average age of 24.4 years. The PBL cohort (N = 95) was 69% female, 84% Caucasian, with an average age of 24.2 years. A 50-question multiple-choice examination covering the basic tenets of medicinal chemistry was prepared. The students were not required to participate in the evaluation. The content topics were taken from across the 2 semester sequence and ranged from electrolyte calculations and molecular weight, to utilization and application of structure activity relationships toward the resolution of therapeutic problems. Our goal was to assess the outcomes of student learning after the first iteration of this format change.

Students were asked not to prepare for the examination and student anonymity was insured. The examination was administered over a 2-hour period. Pretests were given within 1 week of the start of the first semester and the posttests were administered within 2 days of the end of the second semester of the medicinal chemistry course sequence.

Statistical analyses of the examination scores were conducted using the SPSS software package. Comparisons of pretest versus posttest scores for each cohort were conducted using a dependent sample 2-tailed t test with $\alpha = 0.05$. Comparisons were conducted across the cohorts for pretest versus pretest, posttest versus posttest, and posttest/pretest difference versus posttest/pretest difference using independent sample 2-tailed t tests. A Bonferroni adjustment to $\alpha = 0.01$ was made for each of the independent t tests since 3 tests would be conducted on each of the cohorts.

Fifteen questions that required extended thought were selected and the percents of correct responses for each question from the pretest and posttest for both cohorts were tabulated. Extended thought questions were defined by those questions that required the students to use information in new situations or make inferences from that information to solve problems. These skills are defined at the application and analysis levels of Bloom's taxonomy. Analyses of the respective percentages of correct responses were conducted for the examination scores in the same manner as described above.

RESULTS

The posttest scores for the non-PBL cohort and PBL cohort, respectively, were significantly higher than the pretest scores based on the significant p values and the 95% confidence interval of the difference between the means (Table 1). A post hoc power analysis was not conducted because of the large sample size for each test.

The comparison across the non-PBL cohort and PBL cohort, respectively, of the pretest scores revealed a statistically non-significant difference between the scores based on the non-significant p value and the 99% confidence interval between the means (Table 2). The comparison across the non-PBL cohort and PBL cohort, respectively, of the posttest scores revealed a statistically significant difference between the scores based on the significant p value and the confidence interval. This result was confirmed by the posttest-pretest difference of scores comparison across the cohorts. The p value and the confidence interval for the test were significant (Table 2). A post-hoc power analysis was not conducted because of the large sample size for each test.

The posttest percent of correct responses for the extended thought questions for non-PBL cohort and PBL cohort, respectively, were significantly higher than the pretest percent of correct responses based on the p value and the 95% confidence interval (Table 3 and 4). Since n = 15, a posthoc power analysis was conducted.[7] Cohen's d was found to be 3.42, the non-centrality parameter, δ, was 13.24, which gave a power >0.999 for the non-PBL dependent sample t test. For the PBL cohort: Cohen's

Table 1. Comparison of Examination Scores of Pharmacy Students Enrolled in a Medicinal Chemistry Course Before and After Problem-based Learning Was Implemented

Cohort	Pretest Score,* Mean (SD)	Posttest Score, Mean (SD)	Difference in Mean (SD)	p†	95% CI of the Difference Between the Means
Non-PBL (n = 94)	15.6 (3.8)	28.1 (5.8)	12.4 (7.4)	<0.05	10.9 to 13.9
PBL (n = 79)	16.1 (3.5)	24.6 (4.7)	8.6 (6.3)	<0.05	7.2 to 10.0

*Out of a possible score of 50
†The SPSS software returned a p value of 0 for the respective t values. The p values were estimated using a derivation of the t-distribution function for large degrees of freedom.[13] The derivation gave a more conservative p value when compared to using the z tables for a normal distribution. ($\alpha = 0.05$)
PBL = problem-based learning

$d = 0.855$, $\delta = 3.31$, power $= 0.74$. The power of the aforementioned test was slightly lower than the preferred power of 0.80. The pretest versus pretest, posttest versus posttest, and the posttest-pretest difference results, respectively, were statistically nonsignificant based on the p values and confidence intervals (Tables 3 and Table 4).

The Levene's test for equality of variances results did not demonstrate a statistically significant difference between the group variances within each of the respective independent sample t tests. This provides a quality assurance measure that each t test gave a statistically valid result.

DISCUSSION

For the non-PBL cohort the significant average increase in raw score for the pre to the post examination was 12.4. The PBL cohort demonstrated a significant increase of 8.6. There was also a significant increase of 18.3 of percent correct responses from pre to the post examination for the extended thought questions for the non-PBL cohort. The PBL cohort had a significant increase of 16.7. These results suggest that learning occurred in both cohorts (Table 1, Table 3).

Comparison of the pretest results shows no differences between the cohorts. Somewhat surprising was the statistical difference observed in comparing the non-PBL cohort posttest results versus the PBL cohort posttest results (Table 2) and the lack of significant difference in extended thought between the cohorts (Table 3). This suggests that the significant difference in the entire examination seen between the cohorts exists in the basic content and fact portion of the sequence. A number of considerations may explain this result.

The review by Albanese and Mitchell seems to support the difference found between the non-PBL/PBL cohort test results in Table 2 in that the PBL cohort appeared to learn less of the course content. The reason may be twofold: (1) insufficient development of a cognitive framework for basic science; and (2) approximately 20% more time is required to cover content in a PBL course than when traditional course delivery methods are used.[1] The lack of a significant difference found in the extended thought questions (Table 3) is again supported by Albanese et al. They contend that PBL promotes "backward reasoning," a term coined by Gilhooly,[8] which may interfere with efficient problem solving. This notion coupled with an insufficient development of

Table 2. Pretest and Posttest Comparisons Across Cohorts

Test	Cohort	n*	Raw Scores,† Mean (SD)	Mean Diff.	p	99% CI of Difference Between Means
Pretest vs. Pretest	PBL	98	16.1 (3.5)	0.593	0.251	−0.746 to 1.93
	Non-PBL	100	15.6 (3.7)			
Posttest vs. Posttest	PBL	79	24.6 (4.7)	−3.42	0.0003	−5.54 to −1.30
	Non-PBL	94	28.1 (5.8)			
Posttest/Pretest Difference vs. Psttest/Petest Difference	PBL	79	8.87 (6.0)	−3.12	0.003	−5.77 to −0.467
	Non-PBL	94	12.0 (7.2)			

*Differences due to voluntary student participation
†Out of a highest possible score of 50
PBL = problem-based learning

Table 3. Comparisons of Percentage of Correct Responses on Extended Thought Questions (n = 15)

Cohort	Difference in Means (SD)	P*	95% CI of the Difference Between the Means
PBL	16.7 (19.5)	0.005	5.9 to 27.5
Non-PBL	18.3 (20.7)	0.004	6.8 to 29.8

PBL = problem-based learning

a cognitive framework may explain the observed results in Table 3.

Prior to the course sequence redesign, active learning had already been included in about 20% of the medicinal chemistry course sequence. The course sequence previously contained many of the tenets of problem-based learning. These active-learning strategies were successfully employed to reinforce concepts and principles. Our successful utilization of active-learning strategies in the past encouraged us to "push the envelope" in terms of their becoming the primary method of delivery. To this end, well over 50% of the course sequence content was presented in a problem-based fashion, requiring the students to discover information rather than reinforce existing knowledge. This may have been too much of a change for the majority of our students in light of the curriculum and their personalities.

The profession of pharmacy attracts a certain type of personality.[9] In a recent McWhorter School of Pharmacy survey, of 4 possible subtypes identifiable on the Myers-Briggs Personality Indicator, one, "sensing/judging" was identified in over 90% of the student population.[10] A number of broad generalizations about people with this attribute ("sensing/judging") can be obtained from Keirsey.[11] These individuals learn best by experiencing, practicing, and memorizing. Sensing/judging individuals learn best when there is a focused and structured learning environment. They prefer to listen and observe, eg, watch how other people do things, listen to a lecture or presentation, and take notes, especially when expecta-

tions, goals, and standards are clearly presented. As learners, "sensing/judging" individuals are less interested in abstract theories than in factual or practical information. Loose, unstructured teaching with unclear outcomes or with a high degree of experimentation, personal interaction, theory or play does not work well for them. Therefore, the open-ended PBL format seems to be a less than optimal teaching methodology for this personality type.

Along with medicinal chemistry, 2 other sequences in the second-professional year were converted to problem-based learning as part of the Pew grant. The 3 sequences ran concurrently with the students maintaining the same groups in each course sequence. This created an environment with a significant change in workload and an increased need for appropriate time management skills. The 3 sequences used varying styles, formats, and requirements, leading to some student confusion and an inhibition of learning. Student focus group interviews and student-led quality teams (LEARN teams) were utilized to obtain this information.[12]

In summary, the finding of decreased content learning coupled with the needs of the "sensing/judging" personality type for a structured-learning environment and a need for a more developed cognitive framework for learning precludes us from utilizing a PBL approach as the dominant process for classroom presentation.

Armed with this information, substantial changes to the *Medicinal Chemistry* sequence from 50% "pure" PBL to a hybrid approach has been developed. The following are several key features of the hybrid approach:

- To enhance building a cognitive framework, early on in the course sequence the students are taught how to model efficient problem solving.
- The steps are:
  ○ read the problem;
  ○ comprehension of the terminology;
  ○ what information is explicitly stated?;
  ○ what information is implicit?
  ○ review of knowledge base relevant to the problem;

Table 4. Comparisons of Percentage of Correct Responses on Extended Thought Questions (n = 15)

Test	Cohort	Mean (SD)	Mean Diff.	P*	99% CI of Difference Between Means
Pretest vs. Pretest	PBL	34.7 (18.8)	1.93	0.789	−17.9 to 21.7
	Non-PBL	32.8 (20.4)			
Posttest vs. Posttest	PBL	51.4 (20.4)	0.333	0.964	−19.7 to 20.3
	Non-PBL	51.1 (19.3)			
Posttest/Pretest Difference vs. Postest/Prestest Difference	PBL	16.0 (18.9)	−1.20	0.868	−21.0 to 18.6
	Non-PBL	17.2 (20.3)			

- introduction to Plan, Do, Study, Act (PDSA) cycle;
- and then cycle through PDSA until a satisfactory answer is achieved.

- Traditional course delivery methods interspersed with short active-learning sessions are used to deliver some of the more conceptually difficult content areas to help build on the cognitive framework.
- Short pre-lectures to introduce the students to the topic are given before the student groups engage in a PBL session. Short impromptu presentations by the groups and a "wrap-up" by the instructor provide the necessary closure to the process.
- Drug design problems are used in both courses of the sequence to engage students at the synthesis and evaluation levels of Bloom's cognitive domains.
- Student groups give formal Microsoft *Powerpoint* presentations on the problems as a means to enhance and reinforce concepts and communication skills.

CONCLUSION

This approach to using problem-based learning in the *Medicinal Chemistry* course sequence seems to work as evidenced by positive feedback from course, instructor, and LEARN team evaluations. While this approach to problem-based learning is not "pure" PBL, it appears to be a viable method of active learning for our student population. We believe that this method provides both the content and higher-order concepts we desire to instill in our students. We are currently investigating the student-learning outcomes of the current format of course delivery.

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Appendix 1. Assessment instrument sample questions.

Sample Content Questions
Which of the following statements are **TRUE**?
A. A thiol group is the nucleophilic species of glutathione.
B. Acetylation is the major Phase II conjugation reaction.
C. Glucuronidation results in increased water solubility.
D. Methylation is a major detoxification mechanism.
E. A & C

Which of the following statements is **TRUE**?
A. Lente type insulins can be mixed with isophane insulin.
B. Insulin is a basic protein.
C. Insulin consists of four peptide chains.
D. Beef insulin is non-immunogenic.
E. Non of the above.

Sample Extended Thought Questions based on Bloom's Competencies of Application, Analysis and Evaluation.

Please rank the following agents in order of antipsychotic potency.

A. X > Y > Z
B. Z > X > Y
C. Y > Z > X
D. X > Z > Y
E. Y > X > Z
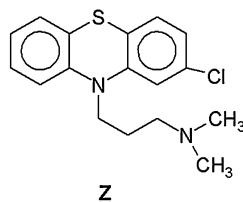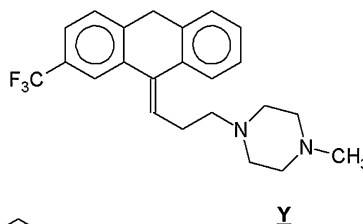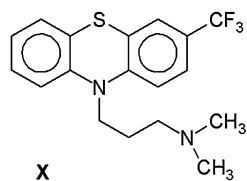
Please rank the following structures in order of increasing diuretic potency.

A. X < Y < Z
B. Y < Z < X
C. Z < X < Y
D. Y < X < Z
E. X < Z < Y