Computer-Assisted Generation and Grading of Pharmacokinetics Assignments in a Problem-Solving Course[1]

Reza Mehvar

College of Pharmacy and Health Sciences, Drake University, 28th and Forest, Des Moines, IA 50311-4055

PROLOGUE

Computer-generated practice problems (with opportunity for unlimited practice) and assignments (with automatic grading by computer) were developed for a problem-solving course in basic pharmacokinetics. For each topic, a problem was developed using the spreadsheet program Excel®. The students, then, used these files to generate their own assignments and practices. Although the general structure of each problem is the same for all generated cases, the problem (including the data and in some cases the text of Questions) is dynamic in that by pressing a button a new problem is generated randomly from a preset range of parameters and/or text scenarios. After working on the generated assignments, the students enter the solutions in the program and electronically submit their assignments to a "Drop Folder" in a "Pharmacokinetics" server using a local network on campus. The received assignments are then graded automatically using a "Grader" spreadsheet developed for each assignment. The project was successfully implemented during the Fall of 1996 in a class of 150 students. Evaluative data indicate that the project substantially improved students understanding of the subject and helped them perform better in formal examinations.

INTRODUCTION

Basic pharmacokinetics is a part of core curriculum in professional pharmacy programs in the U.S.[2](1) and most other countries. Learning pharmacokinetics involves concepts such as volume of distribution and clearance. Additionally, estimation of kinetic parameters from plasma and/or urine concentration-time profiles and design of dosage regimens based on those kinetic parameters are required components of most pharmacokinetics courses. Therefore, besides understanding the concepts, pharmacy students are required to acquire calculation and problem-solving skills to solve pharmacokinetic problems.

Along with the use of examples in the textbooks, pharmacokinetics instructors usually develop their own set of problems and assignments for students. This is a very time consuming task both for development of problems/assignments and, more importantly, for grading them. The latter becomes a major issue especially if the classes are large. One such example is the author's experience at Drake University; during the Fall semester of 1996, 150 students were enrolled in the basic pharmacokinetics course taught to fourth year pharmacy students in the BS program.

Recently, pharmacy educators have used computers to facilitate learning in various disciplines in pharmacy(2-12), a majority of them demonstrating that computer-assisted instruction can improve student learning. As for pharmacokinetics, various computer programs(13-19) have been developed and used for teaching of this discipline. However, all of the available computer-based pharmacokinetic programs used for teaching provide only simulation rather than generation of different scenarios and data. This means that for these programs, students enter kinetic parameters and dosage data, and the program provides simulation of plasma concentration-time courses. These programs are very useful for demonstration of concepts. For instance, the students would be able to see the effects of changes in various pharmacokinetic parameters or dosage regimen data on the plasma concentration-time data. However, the available programs would not allow students to practice and learn how to estimate the kinetic parameters from the plasma and/or urine drug concentrations and how to use these kinetic parameters to design dosage regimens. The latter points are the expected outcomes of most pharmacokinetics courses.

Additionally, an often-heard comment from students is that they are taught contents in the classroom but are evaluated based on actual or simulated problems. This appears to be a valid concern. Realizing this weakness across the curriculum and to be consistent with the recommendations of the Commission to Implement Change in Pharmaceutical Education(1), Drake University College of Pharmacy has adopted a curriculum with problem-solving skills as one of the expected outcomes. This approach again requires development and use of a significant number of assignments and problems in a pharmacokinetics course to give students ample opportunity to practice and be successful. To achieve this goal, computers were used to assist in the development and grading of pharmacokinetics assignments in a problem-solving pharmacokinetics course, the results of which are presented here.

DESCRIPTION OF THE TEACHING INNOVATION

General Description of the Course

Pharmacy 160 (pharmacokinetics) is a required three-credit hour course which is offered to the fourth year students in their BS program. The course is offered during Fall semester with an enrollment of 150 students in the Fall of 1996. The format of the course is centered around a quasi problem-based, objective-driven learning strategy which is described here briefly. For each topic, specific outcomes and objectives are distributed among students. This is followed with a printed problem which captures all of the stated objective and outcomes. To be able to solve these problems,

[1]This article is based on a portfolio submitted to the AACP Council of Faculties and presented during the Innovation in Teaching Awards Special Session, 98th Annual Meeting, Indianapolis IN, July 15, 1997.

[2]ACPE, Accreditation standards and guidelines for the professional program in pharmacy leading to the Doctor of Pharmacy degree, (adopted June 14, 1997).

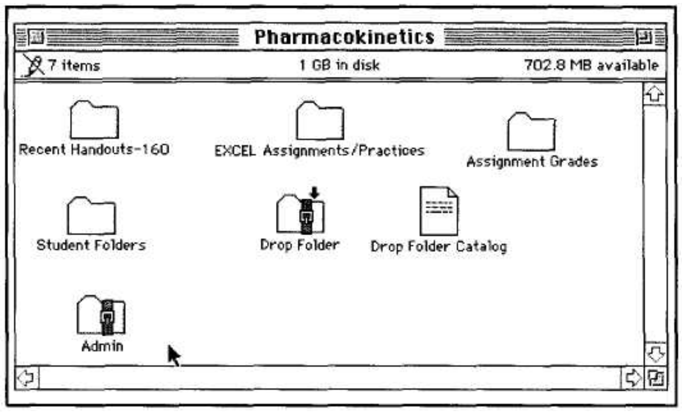

Fig. 1. A screen snapshot of "Pharmacokinetics" server.

Constant IV Infusion
Practice #81

The plasma concentration-time data of kinetophylline after IV infusion of the drug to a 66-kg asthmatic patient as a constant rate of 0.335 (mg/hr)/kg are listed below:

Time (hr)	**0**	**5**	**14.5**	**30**	**49**	**93**
Conc. (mg/L)	**0**	**6.24**	**13.7**	**19**	**20.5**	**19.7**

I. Please estimate the following kinetic parameters of kinetophylline:
1. The steady state concentration(C_{ss})*
2. The elimination rate constant (K)
3. The plasma half life ($t_{1/2}$)
4. The clearance (C1)
5. The volume of distribution (V)
6. A bolus dose if the goal had been immediate achievement of steady state at the start of the infusion

II. After **93** hr of kinetophylline therapy, the patient's condition does not improve. The infusion is discontinued and two post-influsion samples are drawn. Please answer the following questions based on the post-infusion data.

Post-Infusion Time (hr)	**0**	**16.5**	**33.5**
Conc. (mg/L)	**19.7**	**6.19**	**1.74**

1. The elimination rate constant (K)
2. The plasma half life ($t_{1/2}$)

III. The lack of response of the patient to kinetophylline is attributed to the low Css. It is suggested that Css be increased to **32** mg/L. Assuming no drug is left in the body when a new infusion is started, please estimate the following:
1. A new infusion rate (R)
2. The time to reach 90% of steady state (tss) in the absence of a bolus dose (use post-infusion data)
3. A bolus dose to achieve the new steady state immediately

IV. If instead of the rate calculated in III, kinetophylline is infused at a rate of **47.3** mg/h, please estimate the following:
1. The steady state concentration

*Assume steady state if the concentration is ≥90% of the next concentration.

Fig. 2. An example of a printout of the "Data" sheet for the constant IV infusion. For illustrative purposes, the data which are subject to change are demonstrated with bold fonts.

students are referred to a set of reading resources (textbook and/or handouts). The students are required to work on the assigned problem before attending the class session discussing it. After completing the discussion of the topic, students are provided with computer spreadsheets containing practice and assignment problems which are similar to the problem discussed in class. The spreadsheets are used by students for generation of additional practice problems and assignments. The assignments are then submitted for grading.

Outcomes

The computer practice/assignment packages were developed to achieve the following ability-based outcomes in the course:

- Analyze plasma and/or urine concentration-time data to estimate pharmacokinetic parameters.
- Design dosage regimens based on the estimated or provided kinetic parameters.

Electronic Retrieval and Submission of Problems

A "Pharmacokinetics" server (Figure 1) was set up on a computer in our College. Students would access the server using the local network from any computer laboratory on campus. The server contained the assignment/practice files, grade results, course handouts, and any other data which needed to be communicated with students. Additionally, the server had a "Drop Folder" for students to submit their assignments electronically on or before the due date and time. The "Drop Folder" would allow students to submit their assignments while preventing them from accessing the files submitted to the folder by other students. In order to assure students that their file was received by the "Drop Folder", a catalog of all the files in the "Drop Folder" (name of the files only) was also made available to students on the server (Figure 1).

Required Hardware and Software

The practice/assignment workbooks are based on the spreadsheet program Excel® which is widely available on most microcomputers and allows automated tasks via macros written in visual basic language. The same workbooks may be run on both PC (Windows 3®, Windows 95®, or Windows NT®) and Macintosh® (system 7 or higher) platforms with Excel® version 5.0 or higher (including recently released Excel97®). There is no special hardware requirement other than the requirement that Excel® can be run using the hardware.

Description of the Computer Practices/Assignments

For each topic, a problem with a structure similar to the problem discussed in class is developed in Excel®. Students, then, use these files to generate their own assignments and practices. As an example, the computer-generated problem for constant IV infusion is shown in Figure 2. Although the general structure of each problem is the same for all the generated cases, the problem (including the data and in some cases the text of Questions) is dynamic in that by pressing a button a new problem is generated randomly from a preset range of parameters and/or text scenarios (the dynamic data are shown in bold in Figure 2).

When students open each file, an "Instruction" worksheet (Figure 3) would appear, allowing them to select "Go To Practice", "Go To Assignment", or "Exit" the

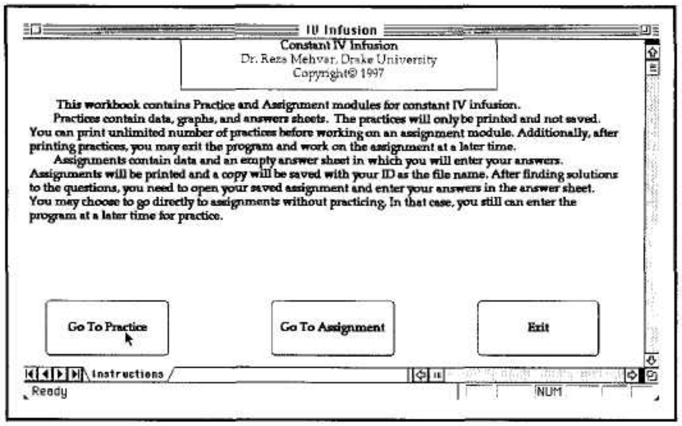

Fig. 3. A screen snapshot of the "Instructions" worksheet

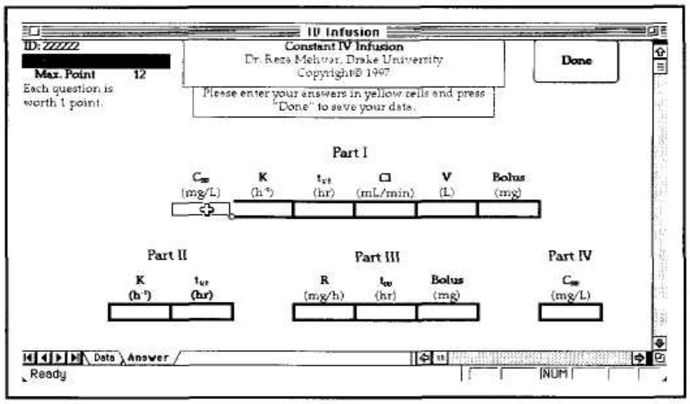

Fig. 4. A screen snapshot of the "Data" worksheet

program using three buttons. Students are encouraged to use the practice module before generating an assignment. When students press "Go To Practice" button, three worksheets ("Data", "Graphs", and "Answers") are opened and the sheet containing the problem set ("Data") is selected (Figure 4). The sheet containing graphs ("Graph") and that containing answers to the posed Questions ("Answers") may be accessed by pressing on the sheet name at the bottom of the screen (Figure 4). There are two buttons ("Generate New Data" and "Select Current Data") on this sheet (Figure 4) as well as on the "Graphs" and "Answers" sheets. Each time a practice or assignment workbook is opened, a random set of data is automatically generated. Students can either select the current data by pressing the "Select Current Data" button or generate a new set by pressing "Generate New Data" button. When they press "Select Current Data" button for practices, a copy of the problem including the answers and graphs will be printed for them automatically. At this point a dialog box would appear allowing students to repeat this process (generating and printing new practices) as many times as they wish. Students may use the data in the practices to answer the Questions and compare their answers and graphs with those provided by the computer in the "Answers" and "Graphs" sheets, respectively.

Once ready, students can generate and work on their assignments. When the button "Go To Assignment" on the "Instructions" page (Figure 3) is pressed, two dialog boxes would ask for the input from the user for his/her name and ID. The assignment workbook consists of a "Data" sheet

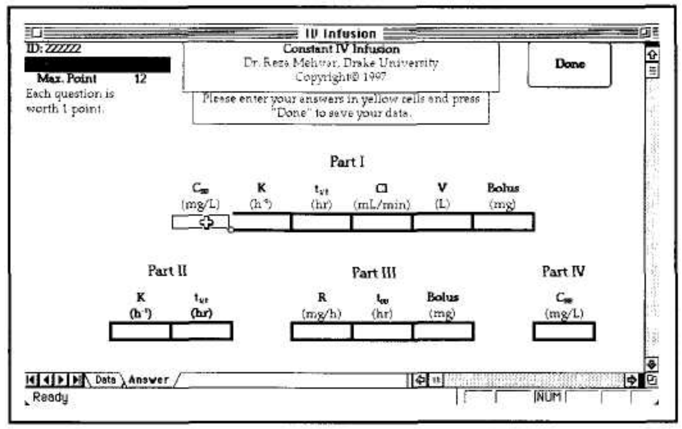

Fig.5. A screen snapshot of the "Answer" worksheet for the assignment.

similar to the practice workbook (Figure 4) and an "Answer" sheet without the solutions (Figure 5). When the student presses "Select Current Data" button for the assignment module, the program automatically saves the selected data with their ID number as the file name and prints a copy of the problem for the student to work on it. In contrast to the original file, the student-selected saved data will be static (the data and text would not change any more). After working on the selected assignment, the student opens the saved file and enters his/her answers in the "Answer" sheet (Figure 5). For the last Fall semester, students were given an opportunity to see their grade as soon as they entered their answers ("Your Grade" in Figure 5). This way, they could rework the problem (if necessary) and find out why they were not receiving the full point value for the problem. After entering their answers in the provided cells, students would press a button ("Done") (Figure 5) which saves their data and exits the program. The completed file can then be transmitted electronically to the "Drop Folder" on the "Pharmacokinetics" server (Figure 1).

Computer-Assisted Grading of the Assignments

Using the program Excel®, a grader was developed for each assignment. The grader would open all the assignments received in the "Drop Folder" automatically and would generate a spreadsheet containing the following: Name and ID of students, a row of answers provided by students; a row of corresponding correct answers generated by the computer; and a row of points assigned to each answer. This data (excluding the name) is then posted on the server for further feedback to students. Grading 150 submitted assignments using a Power Macintosh Model 7100 with a speed of 66 MHz on average would take approximately 15-20 min.

Distinction from Other Available Computer Programs

The available pharmacokinetic programs may be divided into two categories:

1. Those which estimate pharmacokinetic parameters after the user inputs the plasma concentration-time and dosage regimen data. These programs are routinely used in research or clinical practice.
2. Those which simulate plasma concentration-time data after the user inputs pharmacokinetic parameters. These are mainly used for educational purposes to understand the effects of kinetic parameters on the shape of plasma concentration-time profiles.

The developed program is different from both types of

Table I. Student response to Quantitative statements[a,b]

Question		Mean ± SD
1.	Before taking this course, I had used computers frequently.	2.40 ± 1.28
2.	Before taking this course, I had used spreadsheets frequently.	3.53 ± 1.12
3.	Before taking this course, I was familiar with the use of fileservers for retrieval and dropping files.	4.20 ± 1.01
4.	After completion of this course, I have a more positive attitude toward the role of microcomputers in education.	1.67 ± 0.80
5.	After completion of this course, I am less apprehensive about using computers.	2.08 ± 1.07
6.	Access to computers on campus was easy.	3.00 ± 1.31
7.	Once having access to a computer, the procedure for access to the "Pharmacokinetics" fileserver was easy.	1.52 ± 0.77
8.	Having a fileserver for this course facilitated learning.	1.53 ± 0.73
9.	The in-class computer simulations helped me understand the concepts better.	1.91 ± 0.86
10.	I frequently used the spreadsheets called "Practices" outside the class.	2.40 ± 1.27
11.	The "Practice" spreadsheets helped me do better in finishing the computer "Assignments."	2.02 ± 1.12
12.	The instructions for "Practice" spreadsheets were clear.	1.68 ± 0.73
13.	The number of computer "Assignments" were right for this course.	1.71 ± 0.87
14.	The computer "Assignments" reinforced the material covered in class.	1.38 ± 0.62
15.	The instructions for computer "Assignments" were clear.	1.39 ± 0.60
16.	I liked the fact that I could get immediate feedback from the computer regarding my assignment grade.	1.08 ± 0.27
17.	I liked the fact that I had a chance to improve my assignment grade before submission.	1.08 ± 0.27
18.	I liked the fact that I had individualized assignments.	1.28 ± 0.69
19.	I liked the fact that I could submit my assignments electronically.	1.39 ± 0.77
20.	I liked the fact that the results of the assignments were posted within a few hours of due date.	1.25 ± 0.54
21.	"Assignments" improved my understanding of the subject.	1.26 ± 0.55
22.	"Assignments" helped me do better in the exams.	1.33 ± 0.67
23.	The credit for assignments was appropriate for the amount of work done.	1.64 ± 0.95
24.	For me, the time spent on computers in this class was worth it.	1.62 ± 0.99
25.	Overall, the use of computers in this course is worthwhile and should be continued in the future.	1.23 ± 0.64

[a]The scale was 1 = strongly agree, 2 = agree, 3 = neutral, 4 = disagree, and 5 = strongly disagree.
[b]n = 135 students.

programs in that it generates a set of plasma concentration (or urine) time data and/or kinetic parameters and lets the user calculate the kinetic parameters. For problems where plasma concentration-time data are generated (such as the IV infusion problem in Figure 2), a random error of ±10 percent is added to the data in order to make it more realistic. Additionally, the students' answers are accepted within a certain error (*e.g.*, ±10 percent for acceptance of the answers).

Another major distinction between the innovation and available pharmacokinetic programs is that, to our best of knowledge, none of the available pharmacokinetic programs would allow automatic grading of homework.

Advantages and Disadvantages

The advantages are listed below.

- Unlimited source of practice for students: Students can decide how many times they need to practice before they are ready for an assignment.
- Individualized assignment: Each student generates and selects his/her own individual assignment which has a unique data set. Such a system would reduce the opportunity for academic dishonesty which may arise from copying the answers from other classmates when a single set of data is given to students.
- Immediate feedback and remediation: With the option to view their grades, students can rework the problem, if needed, before submitting the assignment.
- User-friendly programs: All students need to do is to work with 6 buttons. They do not even need to have a working knowledge of spreadsheets.
- Minor time commitment by the instructor: Automatic grading will alleviate the problem that most pharmacokinetics instructors are faced with when giving homework assignments.
- Application to other settings: This type of program may be used for self study of basic pharmacokinetics and distance learning. Currently, Colleges of pharmacy are in the process of developing non-traditional PharmD programs for current holders of the BS in pharmacy. Some programs require remediation in basic pharmacokinetics before students are accepted in their PharmD program. The developed programs may be modified for use in these situations.

The programs also have some disadvantages which are listed below.

- Excel® requirement: This should not be a major problem as most computers purchased in academia are preloaded with Excel® software.
- Program Limitations: As with any other educational tool, the developed problems cannot cover all the aspects of pharmacokinetics, especially when verbalization is required. However, the basic calculation skills may be covered in these problems and the rest be left to other instructional tools or pharmacokinetic programs for simulation.

ASSESSMENT OF THE INNOVATION

At the end of semester, a survey was distributed among the students, and the students' perception of the innovation was evaluated in an anonymous manner. The survey was based on quantitative questions using the Likert rating scale. Additionally, three qualitative questions were posed to students.

The quantitative questions and their results are presented in the Table I. As seen from the table, the response of students to the innovation was overwhelmingly positive. The results of Questions 1-3 indicate that while students were using computers before this class, they were not very familiar with the use of spreadsheets and, especially, the use of fileservers on a network. These results are in agreement with previous reports on the computer experience of pharmacy students(7,18).

Generally, most students agreed or strongly agreed that the use of computers in this course helped alleviate their apprehension about computers and made them develop a more positive attitude towards the computers (Questions 4 and 5). Interestingly, despite the lack of a prior knowledge about the fileservers (Question 3), the students strongly believed that their use was easy and facilitated learning pharmacokinetics (Questions 7 and 8). Most students used the practice spreadsheets frequently and agreed that their use was helpful in successfully completing the assignments (Questions 10-12). The responses to all the Questions related to the assignments (Questions 13-23) were strongly positive. Most students strongly agreed that the assignments improved their understanding of the subject and helped them perform better in formal examinations. The ability to receive immediate feedback regarding their grade (Question 16) and to improve their grade before electronic submission (Question 17), however, received the students' strongest approval rating. Overall, most students strongly agreed that the use of computers in this course was worthwhile and should be continued in the future (Questions 24 and 25).

The three qualitative questions were:

1. What was your most favorite aspect of the use of computers in this course?
2. What was your least favorite aspect of the use of computers in this course?
3. How can the use of computers in this course be improved?

The responses to these questions were consistent with those for the quantitative Questions listed above. Generally, in response to Question 1, "immediate feedback" was the most favorite aspect of the computer programs. Other favorite aspects were: opportunity to do "unlimited practice," "learning computers and kinetics together," "reinforcement of topics," "individual learning," "could work at our own pace", and "ability to select your own numbers." For Question 2, "access to computers on campus" was cited most frequently as the least favorite aspect of computer use in Pharmacy 160. Other least favorites were: "time it took to print the graphs" and "time spent" on working through each assignment. When asked about the improvement, most comments centered around improving the accessibility on campus and devising methods for off-campus access (such as access through internet).

Although based on the students perception, the spreadsheets improved their learning of pharmacokinetics (Table I), direct and unbiased performance data are necessary to support this notion. For example, a comparison of the grades obtained in the course in the presence and absence of the innovation over two or more years may be made. For Pharmacy 160, the mean ± SD of scores for 1995 (74.8±12.5; n = 134) was significantly ($P < 0.0001$, unpaired t-test) less than that for the Fall of 1996 (82.6 ± 10.1; n = 150) when the innovation was introduced. Such a comparison would be valid if the only difference between the groups is the presence/absence of the innovation. However, the use of computerized assignments/practices was part of a major change in the course which also included using a quasi problem-based format, instead of traditional lecturing, described earlier in this article. Therefore, the improvements in the performance of students during the Fall of 1996 cannot be attributed only to the use of practice/assignment files. Nevertheless, it is likely that the innovation has had an impact on the improved performance.

PERSONAL REFLECTIONS AND FUTURE DIRECTIONS

The main motivation for the use of computers in generating and grading assignments came from the author's experience with large class sizes (120-150 students in each class) which prevented frequent administration of homework to be graded. This is an important issue, especially for undergraduate institutions which do not have the benefit of teaching assistants available in research universities with graduate programs. What was achieved at the end of semester (see Assessment of the Innovation) surpassed the author's initial expectation of the programs. However, based on the experience gained during the Fall of 1996 semester and the students feedback, some modifications are necessary for the assignment/practice sets to be used in the future.

One of the most frequently cited problems with the assignments/practices has been a lack of access from off-campus locations and the limited number of available computers on campus. A suggestion to improve this problem has been to use internet for distribution of the files. Currently, plans are underway to make these files available on the internet and, more importantly, to allow students to transfer their completed assignment via internet.

Another planned modification will deal with the development of assignment/practice sets for new topics. The topics for which assignment/practice sets have already been developed are as follows: characteristics of lines (slopes and intercepts), rates and rate constants (zero-order and first-order kinetics), kinetics of iv bolus injection (plasma and urine data), kinetics of oral dosing, kinetics of IV infusion, multiple dosing kinetics, dose-dependent kinetics, and physiologic determinants of clearance (clearance additivity, hepatic clearance, and renal clearance). Additional topics to be covered by the assignment/practice sets planned for the Fall of 1997 are bioavailability and bioequivalence, physiologic determinants of absorption, physiologic determinants of distribution, and multicompartment models.

Another shortcoming of the innovation for the last semester was that the assignments/practices underwent several modifications as the semester progressed. These modifications necessitated the use of new or modified instructions for the use of assignment/practice sets and produced unnecessary anxiety for some students. Currently, all the assignment/practice sets are being upgraded for the Fall of 1997. This may reduce the need for extensive changes during the semester.

In conclusion, computers were successfully used to generate pharmacokinetic problems in a problem-solving course taught to pharmacy students in a large class with 150 students. The programs allowed students to have access to unlimited number of practices and provided immediate feedback for remediation of homework assignments. As for the instructor, the development of "Grader" spreadsheets drastically reduced the time necessary for grading of the submitted assignments. Initial assessment of the project suggests that the method facilitates learning of pharmacokinetics by pharmacy students.

Acknowledgment. The author would like to thank Joseph Scavo for setting up and managing the "Pharmacokinetics" server. Also, the patience and cooperation of students who accepted the challenge of working with a new tool to create a more effective learning environment are greatly appreciated.

Am. J. Pharm. Educ., **61**, 436-441(1997; received 9/10/97.

References

(1) Commission to Implement Change in Pharmaceutical Education, "Background paper II: Entry-level, curricular outcomes, curricular content and educational process." *Am. J. Pharm. Educ.*, **57**, 377-385(1993).
(2) Clem, J.R., Murry, D.J., Perry, P.J., Alexander, B. and Holman, T.L., "Performance in a clinical pharmacy clerckship: computer-aided instruction versus traditional lectures," *ibid.* **6**, 259-263(1992).
(3) Vance, M.A. and Hageboeck, T.L., "MicroMouse: computer simulation of quantal dose-response experiments for undergraduate pharmacology laboratories," *ibid.*, **57**, 122-126(1993).
(4) Brimberry, W.M. and Riffee, W.H., "Computers in the classroom: a new form of active learning," *ibid.*, **59**, 1-7(1995).
(5) Harrold, M.W., "Computer-based exercises to supplement the teaching of stereochemical aspects of drug action," *ibid.*, **59**, 20-26(1995).
(6) Kinkade, R.E., Mathews, C.T., Draugalis, J.R. and Erstad, B.L., "Evaluation of a computer simulation in a therapeutic case discussion," *ibid.*, **59**,147-150(1995).
(7) Tysinger, J.W. and Armstrong, E.P., "First-year pharmacy students' computer experience and attitudes," *ibid.*, **59**, 43-47(1995).
(8) Chandra, A. and Holt, G.A., "Need to enhance computer skills of pharmacy students," *ibid.*, **60**, 297-303(1996).
(9) Chisholm, M.A., Dehoney, J. and Poirier, S., "Development and evaluation of a computer-assisted instructional program in an advanced pharmacotherapeutics course," *ibid.*, **60**, 365-369(1996).
(10) Faulkner, T.P. and Sprague, J.E., "Application of several multimedia approaches to the teaching of CNS pharmacology: parkinson's disease and antiparkinsonism drugs," *ibid.*, **60**, 417-421(1996).
(11) Sewell, R.D.E., Stevens, R.G. and Lewis, D.J.A., "Pharmacology experimental benefits from the use of computer-assisted learning," *ibid.*, **60**, 303-307(1996).
(12) Haworth, I.S., Bolger, M.B. and Eriksen, S.P., "Use of computer-based case studies in a problem-solving curriculum," *ibid.*, **61**, 97-102(1997).
(13) Bourne, D.W.A., "MULTI-FORTE, a microcomputer program for modelling and simulation of pharmacokinetic data," *Comput. Methods Programs Biomed.*, **23**, 277-281(1986).
(14) Sullivan, T., "Computer-assisted instruction in pharmacokinetics: the SIMU series," *Am. J. Pharm. Educ.*, **52**, 256-258(1988).
(15) DiFazio, M. and Shargel, L., "A mathematical utility program to facilitate student comprehension of the pharmacokinetics of the one compartment model," *ibid.*, **53**, 50-53(1989).
(16) Sullivan, T., "Use of MathCAD in a pharmacokinetics course for pharmD students," *ibid.*, **56**, 144-147(1992).
(17) LeBlanc, P.P. and Aiache, J.M., "Problem-based and computer-assisted learning of pharmacokinetics," *ibid.*, **58**, 94-95(1994).
(18) Bolger, M.B., "Cyber Patient(TM): a multimedia pharmacokinetic simulation program for case study generation in a problem-solving curriculum," *ibid.*, **59**, 409-416(1995).
(19) Li, R.C., Wong, S.L. and Chan, K.K.H., "Microcomputer-based programs for pharmacokinetic simulations," *ibid.*, **59**, 143-147(1995).