Computerized Medicinal Chemistry Case Studies[1,2]

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PROLOGUE

This paper describes the development of computerized case-study learning tools which demonstrate how scientific principles can be applied when solving therapeutic problems. Ten computerized case studies emphasizing the practical relevance of basic and medicinal chemistry principles to pharmacy practice have been developed utilizing Microsoft Visual Basic 3.0. The cases introduce a patient or clinical situation, and require the student to make a therapeutic decision, a drug product selection, or provide drug information. Utilizing the mouse to indicate answer choices to structured questions, students are guided through the chemical thinking processes required to arrive at the correct therapeutic decision(s). Wrong responses generate questions which guide students in correcting their mistakes, while correct answers are positively reinforced. A tutorial program is loaded with each case study, and is accessible from a pull-down menu. Humor and graphics are utilized liberally to enhance student appeal. The computerized medicinal chemistry case study modules are currently being evaluated on a national scale, and preliminary data indicate they are effective and enjoyable tools to assist students in learning the concepts and practical applications of medicinal chemistry.

INTRODUCTION

There is a movement in contemporary U.S. health science education to emphasize pedagogical techniques which promote problem-based, student-centered learning. Pharmacy education has recently demonstrated interest in the use of case studies to facilitate integration of basic and clinical science principles. (1-13) The most frequently utilized case studies focus on drug product selection and therapeutic monitoring of hospitalized patients. While case studies are certainly an effective approach to the instruction of clinical therapeutics, a broad-based incorporation of this teaching technique earlier in the professional curriculum would serve a number of important purposes. It would be expected to engender analytical thinking and problem solving skills which would be carried through the entire professional curriculum. Professional viewpoints would be stimulated while students are still laying the scientific foundation upon which their clinical expertise will be based. Students would certainly gain a better understanding of how their knowledge of the pharmaceutical sciences can be applied to patient-specific therapeutic decisions. Since the majority of students enrolled in U.S. pharmacy programs plan on becoming practitioners, reinforcing the practical relevance of content should enhance their appreciation for pharmaceutical sciences courses. Students thus prepared would have a more complete understanding of the therapeutic problems they will encounter in clinical courses, on clerkship, and in actual practice.

Computer-assisted instruction (CAI) is the ideal format for the development of case studies which require integration of scientific and clinical reasoning. It permits students to work at their own pace, and advance to more difficult cases when they are ready. Supplementary information to assist students in solving case study problems can be loaded with the program, making a quick review of principles convenient. CAI also frees students from the anxiety of being wrong, since the mistakes they will inevitably make as problem-solving skills develop can be corrected privately.

This paper describes the development and assessment of ten computer-based case study modules which reinforce the importance and appropriate use of basic and medicinal chemical principles in rational therapeutic decision-making. The cases stress the chemical rationale behind drug action and reinforce pharmacologic, pathologic, toxicologic and socioeconomic factors which could impact therapeutic decisions. Our educational goals for the computerized case studies include: (*i*) enhancing critical thinking and problem solving skills in students; (*ii*) demonstrating the practical relevance of basic and medicinal chemistry to the contemporary practice of pharmacy, (*iii*) promoting an appreciation for the scientific rationale behind therapeutic decisions, and 4) increasing student enthusiasm for, and enjoyment of, the study of medicinal chemistry.

DESCRIPTION OF THE INNOVATION

Case Structure and Format

Ten computerized case-studies have been developed in the following topic areas. The number of cases addressing the topic are provided in brackets: acid-base chemistry [2], antihistamines [1], cholinesterase inhibitors [3], muscarinic antagonists [1], alpha [1] and beta [1] adrenergic agonists, local anesthetics [1, this case is the second part of an organophosphate cholinesterase inhibitor case], and targeted drug delivery [1]. The case studies place the student in the role of pharmacist or drug design expert, and present a patient-oriented scenario that requires a therapeutic decision, drug

[1]This work was supported by a grant from SmithKline Beecham and AACP through the Grant Awards to Pharmacy Schools Program.

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

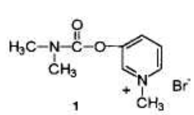
[3]Students participating in this assessment were from Creighton University, St. John's University and the University of Houston.

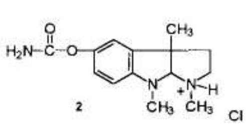
product selection, or the provision of drug information. The cases send the clear message that pharmacists are proactive providers of service to the public and other health care professionals, and have the knowledge base necessary to positively impact patient care outcomes. All cases are written to reflect professional decisions potentially encountered in a variety of settings including, but not limited to, community, institutional, extended care facility practices, and the pharmaceutical industry.

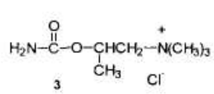
Each case study module, in its entirety, is a multifaceted decision tree. Students are presented with the initial case scenario, and asked an opening key question (*e.g.*, which drug structure of the choices provided would be most appropriate to address a patient's therapeutic and personal needs?). Once an initial response to the opening case study question is selected, students are guided through the chemical thinking processes that allow them to arrive at the correct response. To accomplish this, questions addressing desired or anticipated therapeutic outcomes are posed, followed by answer choices giving chemically-based explanations for these clinical responses. Students are expected to analyze how specific chemical functional groups and/or physicochemical properties influence receptor affinity and selectivity, distribution, metabolic vulnerability, in vitro stability, potential route(s) of administration, and patient compliance. Drug structures, rather than drug names, are provided so that chemical reasoning motivates student response to case questions.

Wrong responses to case study questions commonly generate a series of new questions which guide students in discovering where their thinking went awry. Students who select wrong answers are often encouraged to consult appropriate volumes in the Tutorial Library before continuing with the case. To promote student acceptance of the program, the language utilized in the case study text and in the tutorials is conversational and, when appropriate, humorous. Positive reinforcement for correct responses is the rule. An example of a typical case study scenario follows.

> *As a pharmacist concerned with the health care available to all people, you have volunteered your services in the Dominican Republic through your university's world-wide outreach program. You will be assisting a physician in performing delicate eye surgery on a 74 year old man. The surgery will be taking place in a makeshift hospital in a remote village "campo" and drugs are in short supply. The MD asks you to select an appropriate agent from among the donated drugs to maintain miosis during the operation. She wants the agent to act rapidly upon topical administration and provide a relatively short duration of action so that the extent of miosis can be easily controlled. You brush a lizard off a box marked "Ophthalmics" and find the following carbamate candidates. Let's examine them in light of this patient's therapeutic needs.*


1


2


3

Solving this case requires the student to understand cholinesterase inhibitor structure-activity relationships (SAR), the structural features required for direct and indirect cholinergic action (which requires an in-depth understanding of the chemistry of the muscarinic receptor and the acetylcholinesterase enzyme), the impact of carbamate structure on the onset and duration of cholinesterase inhibition, and the impact of tertiary vs. quaternary amine structure on membrane penetration, systemic distribution and side effects.

A Tutorial Library is loaded with each case to assist students experiencing difficulty with important concepts. The Library contains "volumes" on Acid-Base Chemistry, Physicochemical Properties, Drug-Receptor Interactions, Immunoconjugate Chemistry, and the structure-activity relationships for all classes of drugs discussed in the ten cases. The tutorials are brief, descriptive overviews of information students are expected to receive in class or through reading. Each volume is organized to permit rapid retrieval of selected information. The Tutorial Library is accessed through a pull-down menu. Students can momentarily escape from the case to consult a volume in the Tutorial Library, which they select by using the mouse to "click" on the volume title. The pull-down menus also allow review of chemical equations and the structures of the drug molecules under consideration. Exit from any of these options will return the student to the last case study screen viewed.

The computerized case study problems were developed using Microsoft's Visual Basic 3.0. This program allows ready production of case study disks or CDs, and can run on any computer that utilizes Windows. It is not necessary for the end-user to acquire Visual Basic software. Every time the user launches the program, a welcoming introductory screen appears. This screen acknowledges the support of the SmithKline Beecham Foundation in the development of this teaching/learning tool, and permits the user to select any of the ten cases by clicking on a descriptive title button.

Target Audience

The two computerized cases addressing acid-base chemistry concepts can be used by students as early as the first professional year. To be successful in these most fundamental cases requires a knowledge of functional groups with acidic or basic character, an understanding of how acidic and basic salts are named, and a general understanding of the relationship between molecular lipophilicity and drug distribution. Cases built around therapeutically relevant structure-activity relationships of drug molecules are best mastered by students who have had coursework in physiology and biochemistry, and who have studied or are currently studying medicinal chemistry. A knowledge of basic pharmacology is beneficial, but not essential to the successful completion of the case studies, as pharmacological principles are incorporated in the tutorials. In order to gain the maximum benefit from the cases, students should have been introduced to general principles of pharmaceutical care and therapeutic decision-making, although formal therapeutics coursework is not required to realize value from the computerized case experience.

Use of the Innovation

At Creighton University, all students are admitted to a four year Doctor of Pharmacy professional curriculum after a minimum of two years of prepharmacy studies. The computerized cases on acid-base chemistry are introduced to first professional year students in the required course Introduction to Pharmaceutical Sciences Principles. Cases requiring a knowledge of structure-activity relationships or immunoconjugate chemistry are offered to students in the second professional year through The Chemical Basis of Drug Action course sequence. Creighton students are familiarized with the case study approach to learning medicinal chemistry concepts through "pen and paper" case study problems given as written homework assignments in both courses. Students also work through case study problems orally in a group-based voluntary weekly recitation period.

The computerized cases are maintained on a file server serving 20 plus PCs in Creighton's School of Pharmacy and Allied Health computer laboratory, and students are informed when a computerized case that addresses a classroom topic is available and how to access it. Students are encouraged to work the cases as accurately as possible the first time through, and then to run them again selecting answers they know to be incorrect. When selecting an incorrect answer, students are advised to first think through why that answer would be wrong, and then validate or augment their thinking with the corrective guidance provided by the program when wrong answer bar is clicked. They are also instructed on the use of the Tutorial Library and other pull-down menu features.

At St. John's University, all accepted students are admitted directly out of high school into a five year Bachelor of Science in Pharmacy degree program. Medicinal Chemistry is taught in the fourth year at St. John's, and enrolled students are required to apply chemical principles to solve case-based therapeutic problems. Cases are regularly given both as homework assignments and as examination challenges. While no computer laboratory that can accommodate the cases is currently available for student use at St. John's, the computerized cases have been introduced in class via a laptop computer, and students are encouraged to arrange time with faculty to review them in more detail. Students are also invited to attend voluntary sessions with faculty to run and discuss the computerized cases.

EVIDENCE OF STUDENT LEARNING

At Creighton University and St. John's University

The computerized medicinal chemistry case studies have been used in the Introduction to Pharmaceutical Sciences Principles and Medicinal Chemistry courses at both Creighton University and St. John's University since 1994. Even though initial versions of the cases were relatively rough, formal assessment indicated that students appreciated their value in helping them evaluate the depth of their knowledge of course content, and enjoyed the opportunity to study through use of the computer. The response of students in these early years to the computerized cases was very positive, and their constructive suggestions for improvement led to the addition of a "Previous Screen" option to the pull-down menu and confirmed our hypothesis that the Tutorial Library would be a valuable addition to the case study package.

In January, 1997 a formal assessment of the finalized computerized medicinal chemistry case study modules was conducted with first and second professional year pharmacy students at both Universities. The results of these assessments are provided in Table I. These results show a high level of student acceptance and enthusiam for the computerized cases.

National Evaluation

We are currently engaged in a national controlled study to evaluate the impact of the computerized medicinal chemistry case studies on student learning and problem-solving ability. Faculty volunteers from six Schools or Colleges of Pharmacy are being recruited to work with us in the completion of this project. The participating schools will represent six distinct geographic regions, with half being private institutions.

In brief, faculty coordinators have been instructed to recruit at least twenty students who are currently enrolled in a medicinal chemistry course into the study. Participating students will be assigned to either a control group (who will not be allowed access to the computerized cases) or an experimental group (who will be required to work through the cases). The composition of the two groups will be matched as closely as possible with respect to: (*i*) size; (*ii*) academic performance level; (*iii*) number of degree-holding students; (*iv*) number of students with a preprofessional chemistry degree; and (*v*) gender. All students will complete a demographic questionnaire and an essay pretest case study problem. These essays will be assessed in a blinded fashion by the faculty coordinator, and Likert-scale scores on six specific performance criteria plus overall problem-solving ability assigned. The Experimental group will then work through the computerized cases, all students will complete a posttest case study essay, and the difference in performance on the above performance criteria and problem-solving expertise will be quantified. It is our hypothesis that exposure to the computerized cases will positively impact chemical thinking skills and problem-solving ability in students. Following the posttest essay, the Experimental group will formally evaluate the cases, and all student participants will be invited to review the modules.

At the time of this writing, two schools have completed the study. The case study module evaluation data collected for one of these Schools are provided in Table I. The impact of the cases on student learning will be presented in a subsequent paper when the study is complete.

REFLECTIVE STATEMENT ON THE DEVELOPMENT OF THE COMPUTERIZED CASES

A thoughtful reflection on why the computerized medicinal chemistry case study innovation was developed requires a review of the original objectives of the computerized case study project.

Enhancing Critical Thinking and Problem Solving Skills in Students

Students are admitted to many pharmacy programs based on high preprofessional grade point averages, but these admirable academic performance levels have too often been attained through passive learning experiences and a skill for memorizing factual information. Once in the professional program, students are expected to go beyond simply learning pharmaceutical facts and theories to demonstrating that they can actually use these tools to think critically about drug therapy, and solve or prevent drug-related problems in actual patients. Unfortunately, the transformation from memorizer to critical thinker is an evolutionary one, and students need to be taught the thinking process professionals go through when solving complex clinical problems. The computerized medicinal chemistry case studies were developed as one tool to help students

Table 1. Student Evaluation of Computerized Medicinal Chemistry Case Studies

	Number responding				
	A[a]	B[a]	C[a]	D[a]	E[a]
1. Which case study modules did you complete?					
a. Acid-Base (Amobarbital overdose)	26	27	45	14	112
b. Acid-Base (Vaginitis)	26	30	45	14	115
c. Antimuscarinics (Corneal inflammation)	0	44	0	11	55
d. AchE Inhibitors (Dominican Republic - eye surgery)	0	32	0	11	43
e. AchE Inhibitors (Mother and son - glaucoma)	0	28	0	13	41
f. AchE Inhibitors (Gardener - organophosphate and local anesthetics)	0	37	0	12	49
g. (Adrenergic Agonists (School yard drug deal)	0	37	0	13	52
h. (Adrenergic Agonists (Asthmatic athlete)	0	39	0	16	55
i. Antihistamines (Trucker)	0	32	45	16	93
j. Immunoconjugate chemistry (10 - Edam)	0	4	0	7	11
2. The information contained on each case study screen was... (Please mark all that apply)					
a. too abbreviated for a good understanding of the concepts.	1	1	36	1	39
b. too wordy to follow ... I got lost!	1	6	8	1	16
c. just right.	24	54	2	17	97
3. The graphics contained on the case study screen...					
a. made the case studies more enjoyable to run.	23	59	42	14	138
b. did not add anything to the value of the case study programs.	3	2	2	4	11
c. were distracting to me.	0	0	0	2	2
4. The format of the case study screen (*e.g.*, placement of text boxes, answer buttons, graphics, etc.)...					
a. made it easy to follow the ideas being presented.	25	59	45	19	148
b. was distracting to me.	0	1	0	0	1
c. was confusing to me.	2	1	0	0	3
5. I found the attempts at humor in the case studies (Please mark all that apply)					
a. appealing (*e.g.*, made the cases more fun to work through).	22	57	44	16	139
b. irritating.	0	0	0	3	3
c. intimidating.	1	1	1	1	4
d. ineffective (*e.g.*, not funny).	4	5	0	1	10
6. The case study tutorials...					
a. were a valuable resource in working through the case study problem.	14	40	28	11	93
b. summarized effectively the important S AR of the class of molecules under study.	6	44	22	15	87
c. were written in a style that was easy to read.	12	36	12	9	69
d. were confusing and difficult to follow.	1	1	1	1	4
e. were not helpful.	2	2	3	0	7
7. How did the computerized case study modules influence your extent of agreement with the statement from the previous question?					
a. The cases did not influence my opinion about the statement.	6	20	9	9	44
b. The cases promoted my extent of agreement with the statement.	20	39	36	10	105
c. The cases negatively impacted my extent of agreement with the statement.	0	0	0	0	0

	YES					NO				
	A	B	C	D	E	A	B	C	D	E
8. Do you believe having access to these computerized medicinal chemistry case studies would help students in your school better understand medicinal chemistry?	26	58	44	19	147	0	1	0	0	1
9. Do you believe having access to these computerized medicinal chemistry case studies would help students in your school succeed in medicinal chemistry courses?	25	59	43	19	146	1	1	1	0	3

Table 1. Student Evaluation of Computerized Medicinal Chemistry Case Studies

	Strongly agree					Agree					Neutral					Disagree				
	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E
10. The computerized case studies in Medicinal Chemistry which I previewed...																				
a. were relevant to the information I was taught in my Medicinal Chemistry course(s).	19	54	35	13	121	3	5	9	6	23	0	0	0	0	6	0	0	0	0	0
b. reinforced important medicinal chemistry concepts.	19	50	29	12	110	4	9	15	7	35	3	1	1	0	5	0	0	0	0	0
c. reinforced importance of chemical knowledge in the actual practice of pharmacy.	18	30	20	8	76	8	25	21	6	60	0	5	4	5	14	0	0	0	0	0
d. required me to think beyond the level that was required of me in my Medicinal Chemistry course(s).	2	7	18	5	32	10	21	15	7	53	11	18	11	4	44	1	14	1	2	18
e. were "doable" based on my knowledge of basic and medicinal chemistry concepts.	18	35	12	5	70	8	25	24	10	67	0	0	8	3	11	0	0	1	1	2
f. were readily understandable (in terms of word usage, chemical terms, language).	19	45	20	14	98	7	12	24	4	47	0	3	1	1	5	0	0	0	0	0
g. were easy to follow (in terms of thought processes and ideas).	19	44	25	12	100	7	14	18	5	44	0	2	1	2	3	0	0	1	0	1
h. were fun to work through.	15	38	32	11	96	11	19	13	6	49	0	2	0	1	3	0	1	0	1	2
i. were visually attractive.	17	40	29	9	95	8	18	15	8	49	1	3	1	1	6	0	0	0	1	1
11. How well do you agree with the following statement: "Knowledge of drug chemistry is critical to the optimal practice of contemporary pharmacy."	21	29	22	8	80	5	23	17	5	50	0	6	5	3	14	0	2	1	3	6

"Evaluative data from: Number responding

A Creighton University first year pharmacy students	26
B Creighton University second year pharmacy students	60
C St. John's University second year pharmacy students	45
D University of Houston medicinal chemistry students	19
E Total	150

master the cognitive steps chemically-astute pharmacists take on the path to making therapeutic decisions that are not only clinically rational, but scientifically sound.

Demonstrating the Practical Relevance of Basic and Medicinal Chemistry to the Contemporary Practice of Pharmacy

Unfortunately, the practical relevance of chemistry to the practice of pharmacy is not inherently obvious to most pharmacy students. They don't know why they had to take Organic Chemistry in order to help people, and are initially uncertain as to what they will gain from the professional chemistry courses in their curriculum. However, given that: (*i*) drugs are chemicals, and (*ii*) pharmacists are the drug experts of the health care team, students can't help but acknowledge that pharmacists must also be the chemical experts of the health care team. The computerized case studies were developed to drive this message home by placing the student in the role of pharmacist and, via a thorough and mechanistic analysis of pertinent drug chemistry, guide them through a complicated clinical problem to a successful therapeutic solution.

Promoting an Appreciation for the Scientific Rationale Behind Therapeutic Decisions

Sound therapeutic decisions don't materialize from thin air. They weren't handed down to generations of pharmacists on stone tablets. Rather, they arise when the pharmacist, having identified the optimal outcome for a given therapeutic situation, couples an understanding of patient-specific needs with an in-depth knowledge of how drugs work in the human system. Biomedical and pharmaceutical sciences courses provide the underpinning for rational drug therapy by getting down to the molecular detail of why drugs behave as they do. This knowledge empowers the clinical pharmacist with predictive skills in such areas as drug biopharmaceutical profiles, pharmacodynamics, stability, toxicity, and appropriateness for use in specific patient populations. While many health professions students study biochemistry, physiology, pathology, and pharmacology, only pharmacy students are educated to think chemically about drugs and the therapeutic process. In our opinion, this important skill will be one of the most unique and valuable strengths they'll bring to the health care team. The computerized cases were developed to instill pride in students for their future role as scientifically-grounded health care providers

Increasing Student Enthusiasm for the Study of Medicinal Chemistry

Despite active attempts to create a dynamic classroom environment and to make the subject of medicinal chemis try come alive for students aspiring to be pharmaceutical care providers, some still find the study of this subject intimidating and (dare we say it) boring. The computerized cases were designed to be a fun, as well as effective, way of checking mastery of course content and chemical principles. While many students weary when required to do the same old activities and assignments in traditional classroom settings, most are enthusiastic about computerized learning tools. The students appreciate our efforts to communicate our science to them in everyday language, and relate to the humor, color, and graphics purposefully designed into the cases. It was our intent to show them that chemistry is cool and has so very much to contribute to the patient care process. We believe our innovation accomplishes that, and relate the following story in support of this belief.

When we were demonstrating the case study modules at the recent APhA annual meeting, we lured students to the booth by asking two questions. Have you had Med. Chem.? Did you hate it? When they answered each question with a resounding "YES", they were cajoled into running a case or two. While the students started out skeptical that our program could change their opinion about chemistry, they were universally enthusiastic about its positive impact and potential utility in the pharmacy curriculum when they left.

We learned much about what students like and don't like in a computerized learning tool when we were initially developing the computerized cases. Students don't like dry, verbose explanations of important chemical concepts, so we kept our text screens brief and focused to the point at hand. Detailed discussions of basic and therapeutically relevant SAR were moved to the Tutorial Library, to be accessed if and when the student required a review. We learned that students can become bogged down in a case. Sometime they are thinking so intensely about the information contained on one case study screen (*e.g.*, "the trees") that they lose sight of how they arrived at that point, what question they are trying to answer, and/or what the original case issue was all about (*e.g.*, "the forest"). To address this potential problem, we incorporated a mechanism whereby students can, screen by screen, trace their thoughts back to a point of clarity. We also added a pull-down menu option allowing students to view the pertinent structures in the case anytime they wish. As mentioned, students did like the conversational language, humor, and graphics of the cases.

FUTURE PLANS FOR THE INNOVATION

The first set of ten computerized case studies address a variety of topics commonly taught early in the medicinal chemistry curriculum. We intend to develop additional case study packages that focus on a specific therapeutic class of molecules (*e.g.*, antibiotics, CNS drugs, cardiovascular agents, corticosteroids, etc.), and have begun work on our second series. While we plan to keep the format of future computerized cases consistent with what we have done to date, we are interested in experimenting with animated graphics, film clips, and (possibly) audio communication with student users.

SUMMARY

The computerized medicinal chemistry case studies were designed to enhance critical thinking and problem solving skills in students, demonstrate the practical relevance of basic and medicinal chemistry to the contemporary practice of pharmacy, promote an appreciation for the scientific rationale behind therapeutic decisions, and increase student enthusiasm for, and enjoyment of, the study of medicinal chemistry. A large sample of pharmacy students from Creighton, St. John's, and the University of Houston who evaluated the case study modules found that they meet these outcome objectives at a high level. Computerized case studies have been shown to be an effective and enjoyable way to assist students in understanding the practical importance of medicinal chemistry to the contemporary practice of pharmacy.

Am. J. Pharm. Educ., **61**, 447-452(1997); received 8/11/97.

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