Is it possible to meet the learning objectives of undergraduate pharmacology classes with non-animal models?

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Abstract
Animal use for education and training in university teaching is small compared to that for research but it is still significant, and often unnecessary for many students. Pharmacology is the discipline which uses most animals. A wide range of ‘proven’ non-animal models already exist and there is good evidence that they can be both educationally and cost effective. To further reduce animal use in education it is important to convince and persuade faculty who are the curriculum ‘change agents’ and efforts should be directed towards this through awareness raising, publishing evidence of successful use of non-animal methods in other universities, providing assistance with integration of alternatives into mainstream teaching, and developing new technological approaches to creating the resources which enable faculty to modify content and educational approach and avoid technological redundancy.

Laboratory-based practical classes, in which students conduct experiments on animals or animal tissue, are a central feature of bio/medical degree courses in most countries. Computer-based learning programs, which simulate such experiments, offer a virtual laboratory experience which may meet the great majority of the learning objectives for most students. Faculty need to be made more aware of the possibilities that alternatives afford, and they need to be convinced of their viability. They also frequently express the desire to be able to modify the computer programs to meet local educational needs and this is something that developers of alternatives need to take into consideration. There is now significant evidence that alternatives are able to meet many of the learning objectives though generic and specific laboratory and surgical skills cannot be adequately taught in this way.

Keywords: computer-based alternatives, virtual laboratories, animals in teaching

Introduction
In the UK the use of animals for educational purposes has fallen year-on-year from its peak in 1989 (~12,000 or 0.37% of the total used for research) to a low in 2005 (~1600 or 0.06%). Although this is encouraging, particularly when set against a steep increase in the number of students in the biological sciences (~350% increase between 1983 and 2003), it is still significant. It is also a gross underestimate as current UK Home Office figures exclude animals humanely killed prior to tissue/organ removal for use in teaching. While a number of bio/medical/health and veterinary courses use animals it is pharmacology courses, and to a lesser extent physiology and biochemistry, which are the main users.

Over this same period there has been a significant trend towards making use of IT in teaching and learning (e-learning) and there are now a large number of high quality computer simulations of animal experiments in pharmacology available to teachers. Although these are just one amongst a range of non-animal models designed to teach skills associated with laboratory practicals they have arguably made the largest contribution towards reduced animal use in pharmacology degree courses at least in the UK. Many universities are using these programs in a variety of ways and, as a consequence, a typical pharmacology degree course today is likely to contain far fewer laboratory practical classes which use animals than a typical pre-1990 degree course. However, there is still scope for further reduction in the use of animals in many courses in which pharmacology is a major component, and teachers/faculty are the people who need to be persuaded to introduce curricula changes to accommodate this.

Undergraduate pharmacology courses in the UK
There are more than 20 universities in the UK delivering single honours BSc Pharmacology courses which typically are of 3 or 4 years duration - some have optional/obligatory 1 year work placements many of which provide laboratory experience.
Teaching is mixed mode and blends face-to-face teaching (lectures, tutorials), and laboratory practicals with problem-based learning approaches and student-centred learning often using online resources. There is also an increasing number of joint honours courses where pharmacology is combined with a related science such as physiology or sometimes a non-science subject such as management. In addition pharmacology is an important component in a range of degree programmes: medicine, veterinary medicine, pharmacy, nursing and other healthcare professional courses, biological/biomedical sciences. Although there is wide variation from university to university a single subject degree course in pharmacology will typically contain over 700h of pharmacology teaching over 3 years with the majority being taught in years 2 and 3 (Dewhurst & Page, 1998). The aim of these courses is to produce graduates who:
- have specialist pharmacological knowledge,
- have a range of specialist pharmacological [laboratory] skills,
- have generic, transferable skills to equip them to be life-long learners,
- are equipped to work in the pharmaceutical industry or other research establishments or carry out further training,
- are equipped to benefit from other graduate work opportunities

A survey of the content of 18 UK BSc courses in pharmacology in 1998 (Dewhurst & Page, 1998) showed that there was significant variation from university to university and really there was no clear core curriculum. The time that students spent in laboratory-based practical classes also varied significantly (mean 42h ± 10 S.E.; range 0-145h). Typically students would also develop practical skills in final year projects on which they also spent considerable time (mean 216h ± 31 S.E.; range 0 (library-based dissertation) – 454h).

The British Pharmacological Society (BPS) produced core curricula for the pharmacology content of a number of degree programmes in 2004. Perhaps unsurprisingly, those for medicine, veterinary medicine, professions allied to medicine and pharmacy made no reference to the need for laboratory skills. In contrast the BPS core curriculum for BSc Pharmacology courses recommended a minimum of 120 h of laboratory-based practical work and suggested that it should be distributed through the course of the degree. The aims and learning objectives of practical work may be defined as follows (modified from BPS core curriculum):

**Aims:** to provide opportunities for students to learn, develop and practice:

1. The application of the scientific method and experimental design.
2. Problem-solving skills.
3. Generic biological practical skills (e.g. weighing, preparing solutions, pipetting).
4. Skills in observation, measurement, appreciation of variability, concern for precision, data handling skills: analysis, presentation and interpretation.
5. Oral and written communication skills: report writing, poster production.
6. An appreciation of safety in the laboratory.
7. Pharmacology-specific practical skills.

**Core Objectives**

1. To be able to follow a written schedule in a laboratory setting over a range of methodologies and to know and be able to observe appropriate safety measures to ensure safe working.
2. To be able to prepare accurately appropriate solutions of drugs, to administer required doses and to achieve required concentrations in \textit{in vivo} and \textit{in vitro} situations.
3. To have prepared the apparatus and solutions for and set up at least two different isolated preparations
4. To have determined responses to agonist and antagonist drug administration.
5. To have determined the relationship between concentration and response for an agonist.
6. To have demonstrated and measured drug selectivity.
7. To have experience of the measurement of ligand binding.
8. To have experience of methods of data gathering, data validation, data analysis and data interpretation.
9. To understand and be able to demonstrate principles of good experimental design

The BPS document also cites some more specific objectives including: practical experience of a range of isolated tissue experiments and whole animal preparations, cell culture methodology, electrophysiology, ligand binding, \textit{in vivo} pharmacology, \textit{in vitro} toxicology, immunopharmacological techniques, and animal handling.

Clearly, coming from within the profession, these objectives are important and any non-animal model must demonstrably achieve most of these at least as effectively as the traditional approach, if it is to be considered by teachers as a viable alternative. Although many stakeholders exert influences on the shape and content of the curriculum (the University as the educational provider and owner of the intellectual property rights of the courses; students who pay fees; employers who provide employment...
for pharmacology graduates; and external bodies such as Pharmacology Societies), it is the faculty who develop and deliver the curriculum, and decide the learning objectives and assessments and it is they who, it could be argued, are the primary change agents and who need to be persuaded. The challenge then is to design suitable non-animal models which can meet the learning objectives as far as possible, make teachers more aware of their existence and provide them with convincing evidence of their usefulness.

Laboratory practical classes do have advantages: they promote interactive and active learning; teacher-student interaction; and, at the moment, they are the only vehicle for effective teaching & learning of lab skills, animal handling skills and surgical skills. As haptic and virtual reality technology improves they may one day prove to be an effective way of teaching these skills. There are also disadvantages: they are heavy on staff and student time; expensive in that they require technical support, equipment, consumables, and specialist accommodation which often lies idle for many months; sometimes they provide a negative learning experience for students when an experiment 'fails'; and of course they use animals.

A survey of 52 UK universities (Hollingsworth & Markham, 2006) identified the employment of pharmacology graduates (705 BSc, 36 MSc and 96 PhD) 6 months after graduation in 2003. The proportion of students undertaking further training was 36% (BSc), 34% (MSc) and 4% (PhD). Employment that required pharmacological knowledge was undertaken by 18% (BSc), 18% (MSc) and 67% (PhD). Graduates going into non-pharmacological employment were 18% (BSc), 3% (MSc) and 2% (PhD). The remaining graduates had either gone abroad, were unplaced and seeking employment, unplaced but not seeking employment, or their employment status was unknown. They concluded that a significant proportion of the pharmacology graduates made use of their pharmacological education or were likely to following further training, though only 11% gained employment in the pharmaceutical industry.

Non-animal models

A number of non-animal models exist (see Gruber & Dewhurst, 2004 for review) and are available to teachers: computer programs which typically simulate animal preparations/experiments in pharmacology and physiology; video and interactive video often designed to teach anatomy; mannekins/models/simulators/virtual reality often designed to teach clinical or low level surgical skills; human self-experimentation particularly in physiology where students can perform a range of experiments on themselves or fellow students; use of plant tissues, post-mortem material, and cultured cells; use of ethically sourced cadavers particularly in veterinary medicine; and clinical skills learned and practiced in the veterinary clinic in the treatment of [sick] animals. The focus of this paper is very much on computer simulations which have probably had the greatest impact on animal use in pharmacology education.

Which Teaching and Learning objectives can computer simulations achieve?

There is evidence from a number of studies (Clarke, 1987; Dewhurst, et al, 1988; Dewhurst, et al, 1994; Hughes, 2001; Leathard and Dewhurst, 1995) that computer simulations/virtual labs designed to offer an alternative to the traditional practical class can successfully meet some of the learning objectives. In general these studies demonstrate that learning objectives such as knowledge acquisition, and skills such as data handling, experimental design, communication, and team working may be achieved satisfactorily with alternatives. Additionally the virtual labs promote interactive, resource-based learning and the development of IT skills. Knight (2007) carried out an extensive review of the literature and concluded that the learning objectives of veterinary education may be achieved by using humane methods and also argued that this might be true for other undergraduate programs.

The key to the usefulness of the non-animal methods is the closeness of fit between the educational objectives, the context in which the alternative is to be used, and the design of the non-animal model. Clearly, in a virtual laboratory environment there are certain skills, which some teachers might deem to be essential for pharmacology students, which cannot be adequately taught. These might include generic laboratory skills such as making up solutions of test/control drugs (weighing, pipetting, titrating), setting up and using specific equipment all of which can be taught in laboratory classes without the use of animals. Other skills might be more specific such as animal handling, anaesthetisation, some surgery (perhaps tissue removal, blood vessel cannulation), administering test drugs, monitoring physiological signs, humane killing at the end of the experiment. Really these latter skills can, at the moment, only be taught through animal experiments though of course simulators can be used to practice some of these skills and better prepare students and 3-D virtual reality simulations may one day be able to fulfil this need.

Thus, defining the learning objectives is crucial and if specific laboratory skills, such as those outlined above, are deemed a necessary part of a student's education then alternatives may not be able to meet these objectives. Teachers are the ones who make the decisions about whether animal labs are needed in the curriculum and, if they deem that
they are, they should be required to provide a strong justification, perhaps to an ethics committee, for why those skills are needed and why animal labs are the only way to teach them. It might also be argued that if they are important they should be assessed – in practice this rarely happens in most universities. Many courses retain animal labs to teach principles, factual knowledge and as a vehicle for generating data which can be used to teach data handling skills, communication skills etc. There is no doubt that these learning objectives can be addressed equally well (and sometimes better) using a virtual lab (computer simulation).

Using non-animal models

Virtual laboratories are frequently used as direct replacements for animal labs. Students will work in small groups of two or three, and follow a tutor-designed schedule gathering data from the computer screen in much the same way as they would from conventional data recording equipment. Typically they would be required to complete learning activities which may include multiple choice/true-false questions to test factual knowledge, and data analysis and data interpretation exercises. They may be asked to produce a written report of the simulated experiments, write an abstract, create a group presentation of their findings and deliver it as a poster or oral communication. Some of the computer programs include an 'unknown' drug and students may be required to design experiments (e.g. administer the unknown with selected antagonists/agonists so that they can elucidate what class of drug the unknown is. They also may have to determine suitable drug dose levels, route of administration etc.

Even where it is deemed appropriate by the teacher for the students to take part in animal labs, virtual labs may reduce the number of animals needed by allowing students to design appropriate experiments, determine appropriate dosages in the virtual lab before they use an animal so that they are better prepared. Similarly virtual labs could be used for debriefing students in a face-to-face tutorial situation, as a fallback for students whose animal experiment 'fails' and to enable students to collect data additional to that which they collect from the animal preparation.

Are alternatives widely used?

The evidence is that they probably are but there is room for improvement (see Introduction). There are several reasons: the virtual laboratory may not precisely fit with course objectives; there is undoubtedly resistance from faculty to change and to use alternatives, which however good, were not developed by them; resources are required to implement (e.g. develop support materials for) a new method; and often faculty lack the time and sometimes the skills to successfully integrate a new method into the curriculum.

Experience suggests (Markham et al., 1998) that it is not sufficient for teachers to simply make computer-assisted learning programs, such as those described, widely available to students, over a campus network for example and ask them to use them in an unstructured manner. That virtual lab scenario would be analogous to a real lab scenario in which students were provided with an animal preparation and a selection of drugs and asked to learn something about drug action through non-structured investigation. This latter scenario would not happen – tutors would be present in the laboratory and would provide students with learning objectives, a practical schedule to give structure to the class and some sort of assessment which is often the key to successful implementation (Dewhurst and Hughes, 1999). The evidence is that using virtual laboratories requires a similar tutor-supported learning environment and support materials such as workbooks or study guides, which not only give direction to the class but also allow faculty to take some ownership of the educational process. The support materials may be similar to a laboratory schedule and would contain learning objectives, a series of tasks and exercises designed to focus students on achieving the learning objectives, and some form of assessment. A project in the UK investigated whether providing teachers with a set of exemplar support materials (consisting, for example, of workbooks, self-assessment activities, case-based and problem-based learning scenarios, and assessments) could facilitate integration of CAL resources into pharmacology teaching. The results of evaluation studies suggested that this approach can be successful (Hollingsworth et al., 1999, 2001; Norris and Dewhurst, 2002).

Convincing teachers

The impact the alternatives will have on animal use depends on the closeness of fit of the alternative with the needs of the institution and the willingness of faculty in that institution to integrate the alternative into mainstream teaching. Where alternatives have been developed by a teacher for their own use they are usually well-integrated into the curriculum and they work well in achieving those learning objectives for which they were designed. However, the situation is sometimes quite different when these programs are made available to other teachers who are often resistant to using resources developed elsewhere particularly if using the "alternative" requires more time and effort than continuing to use the animal lab. Many faculty consider alternatives to be inferior, and the introduction of technology-based learning methods to be a retrograde step.

Anecdotal feedback suggests that faculty prefer
web-based resources and would like to be able to customize them to their own needs. To date the constraints of the authoring tools used to create the software make customization very difficult. Developing a workable solution to these problems has now become possible with developments in internet technologies and the concept of digital learning objects and repositories and is the subject of a research project (ReCAL) at the University of Edinburgh (Ellaway et al., 2004). Thus, it is possible to give teachers the building blocks (digital learning objects) and easy-to-use tools to aggregate them and create their own learning resources, obviating the need to use complex authoring software. For example English text could be readily translated into any other language and incorporated into a new resource as required, new experiments could be added (provided the data existed) and unwanted ones could be removed, new animations, video-clips and assessments which suited the needs of the course could also be incorporated.

Persuading faculty to adopt non-animal methods can be difficult particularly when the animal lab is much easier for them to deliver, it achieves the desired learning objectives, and feedback from many students is often positive. There is no single valid strategy to solve this problem in all countries where culture and tradition as well as financial and technical constraints differ greatly. In many parts of the world it is also less expensive to use animals and often there is no legislation governing animal use for teaching. Under these circumstances it is important to:

- Increase awareness and outreach activities so that faculty are more aware of non-animal methods and see that they are being used successfully in similar circumstances by other pharmacologists. Several sources of information about alternatives exist. For example, the NORINA database (http://oslovet.veths.no/norina/) contains information about over 3000 alternative models developed for all levels of education, AVAR (Association of Veterinarians for Animal Rights) provides the Alternatives in Education Database (Alt-Ed), which gives a short description of many models, InterNiche (www.interniche.org) has a book (From Guinea Pig to computer Mouse) detailing numerous alternatives, and the European Resource Centre for Alternatives to animal use in HE (EURCA at www.eurca.org) carries more detailed information about a smaller range of high-quality alternatives (e.g. independent reviews, examples of use, evidence of educational effectiveness (van der Valk, et al 2001));

- Encourage faculty to re-examine the learning objectives of animal labs for different student groups;

- Publish examples of how alternatives have been/are being used in different universities i.e. exemplar good practice 'use cases';

- Develop alternatives which allow faculty to edit the content. This is important as it enables them to gain some ownership of the resources and makes it more likely that they will be used;

- Develop sustainable methods to avoid technological redundancy. Many of the existing computer-based alternatives were developed in the 1990s and while the content is still current, technological advances over the last 15 years mean that in many cases they will not work optimally.

Summary

Animal use for education and training in university teaching is small compared to that for research but it is still significant, and often unnecessary for many students. Pharmacology is the discipline which uses most animals. A wide range of 'proven' non-animal models already exist and there is good evidence that they can be both educationally and cost effective. To further reduce animal use in education it is important to convince and persuade faculty who are the curriculum 'change agents' and efforts should be directed towards this through awareness raising, publishing evidence of successful use of non-animal methods in other universities, providing assistance with integration of alternatives into mainstream teaching, and developing new technological approaches to creating the resources which enable faculty to modify content and educational approach and avoid technological redundancy.

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