281P A COMPUTER SIMULATION OF THE LANGENDORFF HEART PREPARATION TO TEACH THE PHARMACOLOGY OF THE AUTONOMIC CONTROL OF THE HEART TO UNDERGRADUATE STUDENTS

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In recent years a large number of computer programs which simulate undergraduate pharmacological experiments or preparations have been developed and demonstrated to the Society. These may be used to support or in some circumstances replace a traditional 'wet practical' (e.g. lack of technical support or the necessary equipment to enable academic staff to run certain practical classes). Computer simulations are no substitute if animal/tissue handling skills or specific laboratory skills are important learning objectives. However, they can be effective in presenting data in an interactive manner and encouraging students to use it to learn and practice data-handling, data-presentation, data-interpretation and report writing skills.

Here we demonstrate a computer simulation of the isolated perfused mammalian heart preparation (Langendorff heart). Introduction and Methods sections cover the removal of the heart , setting it up to record ventricular contractile force, heart rate and coronary blood flow and the administration of drugs. In the Experiments section simulated data, derived from actual data, is presented on a screen display which emulates a chart recorder. Students 'design' experiments by choosing, from a menu, a range of pharmacological agents which may be administered either alone, or in combination with an antagonist or potentiator. Each trace represents several minutes of recording and thus allows students to access a large amount of data in a short period of time. A facility to compare traces of 'drug X alone' with drug X + antagonist Y or drug X + potentiator Z is available. This allows easy visual comparison of qualitative effects and of course more accurate measurements can be taken from the screen.

The program covers: 1. **effects of drugs**: sympathomimetics (adrenaline, noradrenaline, salbutamol, clonidine, phenylephrine, dobutamine) antagonists (propranolol, yohimbine atenolol, prazosin, butoxamide, phentolamine) potentiators (cocaine); parasympathomimetics (acetylcholine, carbachol, methacholine, nicotine) antagonists (atropine, amitryptyline, hexamethonium) potentiator (neostigmine); cardiac glycosides (digoxin, ouabain); coronary vasodilators (nitroglycerine, adenosine (antagonists: theophylline, dipyridamole), histamine (antagonists: cimetidine, mepyramine), verapamil; **2. effect of ions**: (high and low concentrations of calcium, potassium and sodium);
3. effect of increasing pre-load on contractile (ventricular) force (Starlings Law).

It is envisaged that the program could be used in a number of ways: to better prepare students who will the perform the practical at a later date; to debrief students after they have performed the practical; as a 'fallback' to provide data for students whose experiments were unsuccessful; as an alternative to the practical, though it should be remembered that different learning objectives may be achieved.

282P A COMPUTER-BASED INTERACTIVE STUDENT ACTIVITY TO TEACH THE PROCESS OF DRUG DISCOVERY

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A previous demonstration to the Society (Dewhurst, et al 1998) described a computer-based interactive tutorial designed to introduce the principles of the drug discovery process. This program covered all aspects of the process from selecting a disease area through to safety testing and clinical trials.

We have now taken this a stage further and developed a task-based student activity which takes the form of a 'game' and puts students in the shoes of a project team working for a fictitious pharmaceutical company. They have a brief to identify three potential new medicines to treat prostate cancer (the selected disease area) starting with the Company's library of compounds and an identified target (a key enzyme). The program is written in Macromedia Director version 7.0 for PCs (Minimum: Pentium P75, 8 Mb RAM, Windows 95 or later, double speed CD ROM, 14" colour monitor) and aimed at first year undergraduates, new employees in the pharmaceutical industry and good high school students.

The team have to make crucial decisions at each step of the process. Poor decisions trigger the intervention of a Project Manager who's job is to keep the team within budget and on schedule. He advises the team when he intervenes but also penalizes them with the loss of a 'life'. The team have to complete the task with the loss of fewer than five 'lives'.
The program is divided into four sections: 1. High Throughput Screening – students must decide the number of compounds from the library to test and, using a simulated spread-sheet to help them, decide on the optimum use of resources (human and machine) to complete the task. 2. The Screening Cascade - students have to decide either to develop and carry out the tests in series or in parallel. 3. Compound Profiling - students study the properties (water solubility, toxicity, ionic charge and chemical 'attractiveness') of the small number of families of compounds and singletons and select three to take into the final stage. 4. Animal (*in vivo*) testing - at this stage there are ten potential compounds remaining. Students have to reduce this number to three by eliminating 'candidates' after studying the results of five *'in vivo'* studies in animals: plasma concentration (after oral dosing in mice); target enzyme activity in rats; prostate gland weight in rabbits in which prostate cancer has been induced; tumour cell growth rate; and preliminary safety and toxicity testing.

The emphasis is on reinforcing their learning and highlighting important principles of the discovery process e.g. efficient use of resources, use relatively inexpensive *in vitro* testing for preliminary screening, *in vivo* (animal) studies are expensive, the discovery process is long (several years) and very costly.

Dewhurst, D. G., Oswald, S.,Todd, M.H. *et al* (1998) *Br. J. Pharmacol.* 123, 341P.