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Communicating Our Science to Our Customers: Drug Discovery in Five Simple Experiments

Lesley-Anne Pearson and David William Foley*

Drug Discovery Unit, School of Life Sciences, University of Dundee, Dundee DD1 5EH, UK.

ABSTRACT: The complexities of modern drug discovery – an interdisciplinary process that often takes years and costs billions – can be extremely challenging to explain to a public audience. We present details of a 30 minute demonstrative lecture that uses well known experiments to illustrate key concepts in drug discovery including synthesis, assay and metabolism.

A recent Viewpoint[1] in this journal issued a call to arms for scientists, especially those working in drug discovery, to engage with the wider community; extoling us to fill the gaps in knowledge that leave room for misinformation and doubt; and to take seriously the concerns and questions of our ultimate customers. This is a call that we ourselves feel most passionately about. We too understand that 'open sharing' of science cannot stop with our scientific peers, but must include those with whom we do not share a common understanding of technical terms.

Our colleagues highlighted previously the contributions made by our cyberspace advocates, who use online blogs and forums to debate, inform and defend the public from some of the more spurious pseudo-scientific claims and conspiracies, but what of real world public engagement? As stated by our colleagues and evidenced by the recent RSC report on Public Attitudes to Chemistry,[2] the public at large are not anti-science *per se* and are in fact keen to understand the fundamental process that govern the world around us. Their desire to engage with and understand science is also supported by the myriad of successful science festivals/weeks held in cities around the world. Whilst these events tend are typically aimed at enthusing the public about science generally, surely the exciting world of drug discovery has a place at these real world events, in addition to our virtual presence?

Drug discovery is a lengthy, complex and expensive task with a high failure rate. Equally, outreach can be seen by many as a time-consuming, complex task that delivers little in return. The private sector in particular may struggle to justify spending resources in this area, ahead of meeting critical project milestones. However academics in drug discovery, a growing sector, have much stronger incentives to conduct outreach and engagement: not only does it help with student recruitment, it is often a condition of our public sector funding. Whilst academics still relative new-comers to drug discovery, we are old hands at outreach and opportunities exist for academics to support industry in this area.

The challenge of explaining the drug discovery process to a general audience can seem daunting. How can we possibly hope to condense such a lengthy, iterative and interdisciplinary process into a format suitable for presentation to a public audience? When we understand so little of the biology underlying health and disease, are we even qualified to "preach" to the public about what we do? At the University of Dundee, we previously delivered majopr outreach activities focused on our research strengths, including Magnificent Microbes and Bacterial Biocities.[3,4] The DDU therefore set itself the challenge of capturing the essence of drug discovery in a 30 minute demonstrative lecture. Our idea involved identifying the key concepts and using well-established demonstrative experiments to illustrate (Table 1).[5] Each experiment was selected to be visually captivating (that 'wow' factor!), but also to be accurately, or at least appropriately illustrative. We may have simplified in the extreme, but we hope to never lie or patronize the public. We include a brief discussion of the experiments for interested readers and are happy to enter into correspondence with those who require more information.

Table 1 An overview of the Drug Discovery in Five Experiments Public Engagement Lecture

Process	Experiment
What is a disease and what is a medicine?	Malonic acid clock with salt quench
(Iterative) Organic synthesis	Aldol reaction of cinnemaldehye with acetone in ethanol
Biochemical Assay	Iodine clock experiment at two different concentrations
Physicochemical properties	Effect of dry ice on aqueous pH and solubility of polystyrene in acetone
Metabolism	Elephant's toothpaste (or iodine snake) decomposition of hydrogen peroxide using yeast as the catalyst

What is a Disease/Medicine This first experiment is key to setting the tone of the lecture and adjusting according to the audience. For example, the use of the word "drug" instead of "medicine" is ill-advised in some circumstances. The classic oscillating oxidation reaction of malonic acid with potassium bromate is used by the biologist to exemplify concepts of cell signaling, both in healthy and diseased states. This allows us to explain the process of target validation in a simplified and visual manner. Salt (which interrupts the oscillation) takes the place of a medicine in our analogy, selectively blocking the signal and thus "curing" the disease.

Organic Synthesis Once the biologist has demonstrated how drugs work, the chemist illustrates the process of producing one. While the medicinal chemist strives to avoid making such a classic example of "brick dust" in his daily work, the robust condensation reaction of cinnamaldehyde with acetone neatly illustrates the concept of synthesis. A Lego brick analogy is used: by understanding some basic rules and using some imagination, we can create objects with many different shapes and properties. Similarly, applying the rules of organic chemistry allows a wide variety of molecules with different shapes and properties to be synthesized. Here, we begin to introduce the

concept of multiple property optimization that is required for successful drug discovery, which we build upon throughout the talk.

Biochemical Assay Of course, a key property in any drug discovery project is potency. Segueing neatly from the previous experiment, the biologist explains to the audience the challenges of finding out if a molecule we know nothing about can inhibit the action of an enzyme that is too small to see! We use the classic iodine clock reaction to demonstrate a biochemical assay. The reaction is carried out simultaneously at two different concentrations, resulting in a temporally staggered color change. The audience participates by counting the time until the color change. The time difference allows us to discuss how these assays enable identification of the most potent molecules in a screening or optimization campaign. We have also used samples of GFP and UV light as well as the chemiluminescent oxidation of luminol by hydrogen peroxide as variations to this demonstration.

Physicochemical properties A successful drug requires a balance of properties beyond potency. A medicine must be soluble, stable to a variety of enzymes, and able to cross lipophilic membranes. By adding universal indicator to alkaline water and acidifying by addition of dry ice, we are able to highlight changing pH and compare this to the different pHs in the stomach, intestine, and blood. The chemist demonstrates lipid solubility by dissolving a coffee cup with acetone, which allows us to highlight the need for successful drugs to be soluble in both aqueous and lipid environments.

Metabolism Another key property in drug discovery is metabolic stability. The biologist uses yeast as a "liver substitute" in the catalytic decomposition of concentrated hydrogen peroxide. The discussion touches on important topics such as dosing schedules, toxicity, etc., with food digestion and waste as an easy lead into the concept.

In addition to the specifics of the lecture there are a number of additional learnings that can be taken from it. The show is highly adaptable to accommodate groups of different ages and scientific literacy. It can also be performed in a wide variety of locations including schools and community centres thus offering us the change to take drug discovery out of the lab and into the community. The "flow" of the demonstrations reflects the drug discovery cycle and the interplay between the biologist and chemist lecturers mirrors this key professional relationship also.

Feedback has been overwhelmingly positive and engagement is high, with audiences of all ages enjoying the show. Afterward, they are left with a better understanding of the highs and lows of the drug discovery process, and certainly take away key messages related to time, teamwork, and cost.

Public outreach is not a chore, but rather an opportunity to craft a truly meaningful interaction with those who have the most to gain from our work. As drug discovery scientists, we have one major advantage when communicating our work to the public: they are already familiar with medicines from their bathroom cabinets. What they are less familiar with are the cost and time required for successful drug discovery. The onus is therefore on us to communicate these complexities, particularly in academia where most of our funding comes from the public purse. If the public do not understand that it can take 15 years to develop a new drug, then how can they grasp the urgency of funding research into new antibiotics today? We offer our show to the drug discovery community for use and adaptation, to foster and encourage more engagement of the public with our science.

AUTHOR INFORMATION

Corresponding Author

* d.w.foley@dundee.ac.uk

Notes

Views expressed in this editorial are those of the authors and not necessarily the views of the ACS. The authors declare no competing financial interest

ACKNOWLEDGMENT

The DDU is funded by various charities and industrial collaborations. The opinions expressed in this viewpoint are those of the authors and do not necessarily reflect those of the University of Dundee, our funders or collaborators.

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