The first purified chemical compound to be used as a drug is believed to be digitalis obtained from foxgloves in the mid 18th Century.

Where will our

A view from one of the drug discovery teams at the University of Strathclyde, Glasgow, Scotland

Earlier this year I completed a three-year term as a 'Public Partner' on the Scottish Medicines Consortium (SMC), which is the body that advises the National Health Service in Scotland on the cost effectiveness of medicines. My job was to make sure that the patient and the public had a voice in the debates. With that in mind, my blunt answer to the title question is that I don't care, provided that the new medicine is effective and safe. However working also in early stage drug discovery (at the University of Strathclyde, Glasgow, Scotland), I must have a starting point from which to begin the search for a new drug. In the history of therapeutics, many things have been used as medicines: plant and animal products, microbiological products, synthetic compounds including both small organic molecules and large proteins, and even a few elements. Almost all of these possibilities remain viable today but different people take different approaches.

Some pharma companies specialize in proteins, the so-called biologics. This is the most recent source of active compound to reach the market and has had an impact chiefly in the therapy of cancer and inflammatory disease. My experience on the SMC showed that these medicines were high cost, often required out-patient care for administration, and were

new medicines come from?

sometimes challenging with respect to side effects. Other companies maintain an emphasis on small, organic molecules as the active ingredient. Indeed there are pressures for the size of molecule to become smaller in order to get the best value for a drug. Cost and side effects matter with these compounds too. Outwith western industrial pharma an answer from an Indian physician might be "Very little, actually. We've have plenty of good drugs from Mother Nature in our traditional Ayurvedic medicine".

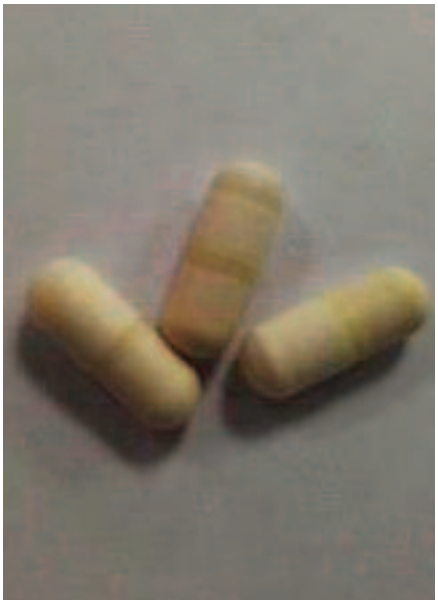
Everybody can't do everything and companies need to make choices but we can't afford to ignore any viable possibilities as a scientific and industrial community interested in improving health and well-being. There's no doubt that drug discovery is more difficult than it once was for many reasons including an increasingly challenging regulatory environment, a lack of good druggable targets (all the easy ones having been done), increasingly challenging disease states associated with aging populations, a lack of good quality new chemical entities, and so on. Overall an intrinsically risky business has become riskier.

Now as an academic, one of my principal concerns is to create opportunity from my research, specifically in the field new small molecule chemical entities for new drugs; most of the work in my labs concerns designed small organic compounds. Our central scientific input is the mature field of heterocyclic chemistry, which, almost uniquely, is able to bridge creatively chemistry and biology and to connect further with medicine. So I make no apology for plugging a science that still makes a difference at the cutting edge. We must continue to teach and train young scientists in chemistry so that they can translate its powerful methodology and creativity into products containing new chemical entities that will make a difference.

No surprise, therefore, that having found something new with potential, I'm very keen for it to be developed towards the market and happy to play an appropriate role in that. Gratifyingly I can speak to several new opportunities from my lab in immunomodulation, cardiovascular disease, and most significantly in anti-infective compounds where we have a new antibacterial compound that has entered phase I clinical trials developed by our partner company, MGB Biopharma in a formulation designed to treat Clostridium difficile infections. MGB Biopharma has also developed an intravenous formulation for the treatment of other Gram-positive bacterial infections building upon basic science from the University of Strathclyde [see http://www.mgb-biopharma.com].

MGB-BP3 is the first in a line of new anti-infective compounds that ultimately work by controlling gene expression by binding to the minor groove of DNA in the target organism, according to the best evidence we have. It's one of a family of compounds that we call Strathclyde MGBs (S-MGBs). We now have S-MGBs that are effective against a wide range of infectious organisms in particular Gram-positive bacteria and trypanosomes, the disease causing agent of sleeping sickness. We've been able to make such progress and to create such impact for several reasons. Firstly the S-MGB platform uses very flexible heterocyclic chemistry so that we can tune the properties of our compounds to target different pathogens whilst remaining safe for the infected host. Secondly, we have strong team-work between many academic colleagues in chemistry and biology at Strathclyde but also at the University of Glasgow. Thirdly, we've worked in partnership with MGB Biopharma; the company's ability to raise funds in a difficult economic climate and to drive through the development programme for MGB-BP3 has been extraordinary.

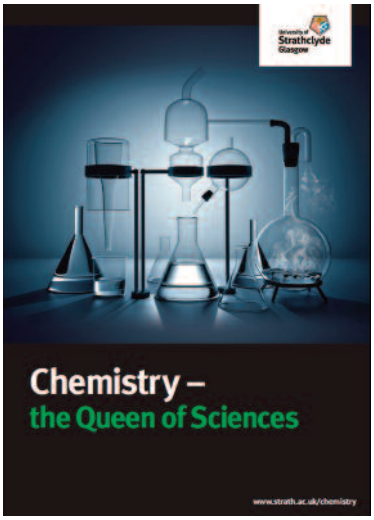
The outcomes of our research are not just the important practical applications but the advancement of the underlying science. For example, we are developing new chemical technologies to synthesise the compounds we need to evaluate. Also in studying the effect of our drugs on the target bacteria and parasites we are discovering more about the internal workings of the infectious organisms. With such information available we would hope to devise new and more effective drugs for infectious disease.



Caption Left: MGB-BP3 formulated in capsules for treating Clostridium difficile. Right: a freeze-dried sample of MGB-BP3 for reconstitution as an intravenous medicine (courtesy MGB Biopharma).

So what does a heterocyclic chemist do to create opportunities for new drugs? Firstly, there has to be a promising and preferably novel starting point, which could be a new compound discovered by screening, usually plant or microbial products or occasionally a compound from animals, or it could be a molecular hypothesis. This is not new at all. In fact it's what has been done ever since chemists got into drug discovery. The new thing, however, is the stringency with which 'promising' and 'novel' can be defined. 'Promising' may relate to an unmet need in medicines currently available. 'Novel' may also reflect unmet need but will also concern the chemical class of compound being investigated. From there, the chemistry-biology interface is so much better developed now that a good deal can be discovered about important things like selectivity and toxicity before a synthetic chemistry programme is begun.

Choosing what to make and how to make it with due regard for the probability of a successful development and for chemical novelty is then the key contribution of the heterocyclic chemist. This is the essential link that both mediates between chemistry and biology and also creates the therapeutic opportunities through the new compounds that emerge. What makes today's science so exciting is that the tools and techniques that we have the power to explore the most detailed properties of molecules and the intimate workings of biology. This means that the coupling between chemistry and biology that is essential in drug discovery is stronger than ever before and is why we place such an emphasis on scientific teamwork at Strathclyde, as is discussed in my e-book which also gives more details of our projects and our approaches through heterocyclic chemistry [see "Chemistry, the Queen of Sciences" available here from the Adjacent Government website.



Cover page of my e-book, which describes in some detail the approach we take to drug discovery using heterocyclic chemistry. An editorial from the Royal Society of Chemistry provides a supportive context.

An overview of drug discovery at the University of Strathclyde can be found in the brochure 'New Medicines, Better Medicines, and Better Use of Medicines', which is accessible on the Stakeholder website of Adjacent Government.

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