

We can get by with a little help from our friends

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Editorial

Received date: 04/11/2016

Accepted date: 05/11/2016

Published date: 05/11/2016

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EDITORIAL

With this editorial I am delighted to contribute to the launch of Research and Reviews: Drug Delivery. I would like to take this opportunity to reflect on how we within the pharmaceutical sciences have to date built the platform from which we now operate, the complexity of contributions and interdisciplinary team work needed to take a drug from concept to clinic and also highlight the important role of pharmaceutical formulation science where I myself operate.

We as a species have come a long way and achieved many great things since our initial evolution from the primordial soup, we are however, although some may hate to admit it, not perfect. Our physiology is a highly complex, finely balanced conformity of processes operating within a frame of reference we consider the normal. Should we stray from this but a little, the smooth operation of our intertwined systems will begin instead to unwind, the consequence of which can be absolute and final. Outside of our normal frame of reference we enter into what is of course the realm of pathophysiology, the disease state and the driving force behind the sciences which contribute to modern drug development. The cause behind such deviation to pathophysiology can take many guises and it is due to the almost limitless complexity of disease that such an expansive and diverse set of disciplines must pull together and contribute to the pharmaceutical sciences if a solution is to be found allowing order to be restored.

Since the dawn of civilization humans have sought to combat disease and promote health by utilizing the products of the world around them ^[1]. Ever since prehistoric times there has been a focus on spiritual healing but more recent times has seen medical interventions rise to the forefront ^[2]. The first physiologically active remedies were most likely plant or herb based, discovered by dogma rather than any process resembling scientific principle ^[3]. This is a status reflected through history with the Egyptians ^[4], Greeks ^[5] and Romans ^[6] providing evidence of early diagnosis and treatment. Some ancient remedies may not seem remote when compared with what has been used in recent times where plant based remedies were implemented such as Aloe Vera ^[7] and camomile ^[8] but of course the weird, wonderful and dubious were also used highlighting a lack of knowledge surrounding the function of the body at such times. Particular interesting ingredients such as worms, dung, urine and even moss from a dead man's skull have graced literature in the past ^[9]. Thankfully more recent times has seen progress made and pharmacology emerge as a science, here attempts are made to describe how drugs work rather than simply explain what they do ^[3]. The 18th and 19th centuries saw the advent of vaccinations ^[10], advances in cellular biology and the understanding of the microbiological basis of disease ^[11], elsewhere, important advances were also seen in chemistry allowing for structural understanding of drugs on a molecular level ^[12] as well as techniques to isolate and purify active ingredients from plants ^[13]. Such developments were now being made on the basis of experimentation as we know it today.

With the advent of the 20th century, significant advances in technology, manufacturing and scientific understanding rapidly accelerated developments in the pharmaceutical sciences. Advances in physiology, notably the identification of chemical signaling, hormones, neurotransmitters, inflammatory mediators and their associated receptors ^[3] coupled with the emergence of Biochemistry, yielded an understanding of enzymes and biochemical pathways and provided the basis for drug targeting ^[14]. This truly revolutionized the pharmaceutical industry which has been enhanced by the ability to generate synthetic drugs though advances in synthetic chemistry ^[15]. This period was to change pharmaceutical approaches forever. The identification of local anaesthetics, antimicrobials and later antibacterial drugs, notably the development of sulphonamides and penicillin were all advances seen in the early 20th century ^[16]. Advances have of course continued at great pace and increases in computing power as well as combined efforts applied in a multifactorial approach to advance the pharmaceutical science has seen phenomenal advances, breakthroughs and increased contribution to understanding from disciplines such as; pharmacokinetics and ADME

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profiling, biochemical pharmacology, systems pharmacology, molecular pharmacology, formulation science, immunology, microbiology, genetics, genomics, metabolomics, clinical contributions and toxicology amongst many others^[3,17]. Together we are now achieving advances in developing diagnostic tools and treatments for high profile disease such as Cancer, Alzheimers, Heart Disease, Diabetes, COPD, HIV/AIDS and many more which tend not to find themselves in the spotlight^[18]. We are identifying new drug targets and new drug molecules through a multitude of high throughput techniques, we are able to optimize existing drug molecules and excipients included within formulations to promote better safety profiles, better efficacy and better pharmacokinetic behaviour in turn improving the all-round performance and desirability of a drug product^[19].

Today's landscape in the pharmaceutical sciences arena is highly diverse and strewn with challenges to be overcome. This presents opportunities to achieve real progress but this diversity means that researchers will operate within their specialized area and contribute to the overall development pipeline, rather than following drug development from concept to clinic as may have once been the case. One such area of specialism is that of formulation science and that is the core element of my particular research area. To be successful here it is imperative to draw from many of the disciplines which contribute to drug delivery and the pharmaceutical sciences as a whole. With a focus on the drug delivery system, there is little or no point in progressing through the drug development pipeline^[20], successfully identifying a drug target and a lead compound in the drug discovery stage if it is to be subsequently formulated in a suboptimal fashion thus limiting its efficacy or range of use. In order for an optimal formulation to be produced, pre-formulation studies are first carried out determining parameters of the drug profile such as molecular weight, solubility, pKa, partition coefficient, drug stability and excipient compatibility^[21]. This information then guides the development of the dosage form as it continues through pre-clinical development.

The route of administration and the particular dosage form used are of paramount importance if the formulation is going to be capable of successfully delivering a drug molecule to its site of action. The main routes of drug administration are Oral, Ocular, Otic, Nasal, Intravenous, Intramuscular, Subcutaneous, Vaginal, Rectal, Topical and Transdermal^[24]. The route of administration will be governed by the anatomical and physiological location of the drug target but there may be more than one route which can be explored. For example intravenous injection and oral administration both have the capability to deliver drug molecules into the systemic circulation. Oral administration is often preferred as it is more patient friendly but it will achieve lower bioavailability than intravenous injection^[22]. For each route of administration there are then a range of associated dosage forms and each brings with it advantages and disadvantages over the others. These are the primary considerations when developing a formulation. Once a route of administration and dosage form has been selected then formulation development moves towards excipient selection and formulation assembly^[21]. Again this is governed by information generated during preformulation studies and is also dependent upon the route of administration. Additional considerations are also brought in at this stage with options for the development of controlled release formulations for example and the fine tuning of the delivery system to best achieve maximum drug efficacy whilst also delivering an elegant formulation which will be well accepted by the patient population^[23]. Once the formulation has been developed and produced stability is confirmed prior to the drug moving on to the next stage in the development pipeline, most likely *in vitro* testing to predict *in vivo* performance^[24].

Although no doubt, I have provided here only a brief insight, I hope I have drawn attention to the complexity in our field and conveyed that we stand on firm foundations. The sciences which contribute to drug development we have at our disposal today are highly advanced and they are the product of an age old developmental pipeline. We as the scientists of today, whatever our specialism, find ourselves at the cutting edge of research and it is only through working together, timely publication of our research, collaboration and promotion of interdisciplinary cohesion that we will make the jump to the next level and achieve the next big breakthrough. Be that improving drug performance, patient adherence or compliance, developing cures or treatments for existing and emerging diseases or improving diagnostics, there is a lot still to be done. With modern technological capabilities and the wealth of information we have available at our fingertips we have never been better placed to tackle the challenges we face. It is often easy in our day to day work to forget just how advanced and at times utterly brilliant the research going on around us truly is and what it has taken to get here. Do not forget that what was considered impossible only a generation ago is now routine and there is no doubt that some of the things we consider impossible today, if we have considered them at all, will be common place for the next generation. I for one look forward to seeing where this journey will take us.

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