Editorial

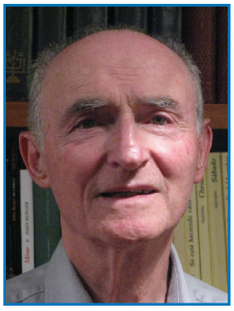
Pharmaceutical BIOPROCESSING

Pharm. Bioprocess.
(2013) 1(3), 217–219

The biotechnology revolution and the education of future professionals in pharmaceutical bioprocessing

The development and industrial-scale production of the next generation of novel biopharmaceutical products is a challenge we must be ready to meet.

Keywords: bioprocess development, biotechnological processes, pharmaceutical engineers, pharmaceutical-plant design, professional education



Jose C Merchuk
Author for correspondence:
Azrieli College of Engineering, Jerusalem, Israel
Ben-Gurion University, Israel
E-mail: jcm@bgu.ac.il

Amir Toren
StarletDerma Inc. 8 HaEshel Street, Caesarea, Industrial Park (South), Israel

Ancient civilizations did not grasp the mechanisms underlying the operation of the human body, which were unveiled relatively late in the history of man. Yet the use of medicines to treat diseases is as old as man is. The shaman healers used to invoke supernatural forces, but also used elements taken directly from their environment to alleviate illnesses. Evidence of pharmaceutical treatments can be found as early as in the bible, as well as in other ancient texts. It may be assumed that the selection of the primeval medicines followed a trial and error procedure. Eventually the cure to a specific disease was found, which then became canonic. The medicines were mainly obtained from plants and herbs, but the specific active component remained unknown. Healing knowledge was inherited from a master by worthy apprentices. With the development of knowledge and understanding of body functions and mechanisms, coherent explanations for healing processes were better defined. The gradual unveiling of the chemical composition of medicines, and especially of the chemical content of medicinal plants, led to the discovery of the correlation between molecules and their effect on specific target organs and illnesses. These gradual processes grew side-by-side with the accumulation of chemical and physiological knowledge. The quantum leap, however, was in the concretion of a novel strategy: identification of the mechanism of the chemical reaction controlling a process, identification of the specific molecular site responsible for the desired reaction, followed by a chemical synthesis of molecules with a structure containing the active region. The understanding of the relationship between structure and function made possible the targeting of certain molecular structures with therapeutic potential. Combinatorial chemistry and monoclonal antibody design played a substantial role in this phase, allowing the screening and the identification of the most active between myriads of possible structures. Drugs are produced by controlled procedures and well-defined protocols. Biochemists and pharmacologists collaborate with engineers in the development of pharmaceutical products and the processes needed for their manufacture.

Recently, a new term was introduced into this equation. Biotechnological research has rendered an exponential growth in our knowledge of the biochemical mechanisms beyond the synthesis of large organic molecules. The recent success of genetic engineering provides new and powerful instruments for the production of complex molecules. It allows harnessing the exquisite synthesis accuracy of living cells for the production of proteins that are precious components of the pharmaceutical arsenal in the fight against complex diseases.

Due to these fundamental developments, a growing number of chemical and especially pharmaceutical companies are taking deep interest in the industrial biotechnology field.

FUTURE SCIENCE

10.4155/PBP.13.30 ISSN 2048-9145

Global companies are acquiring biotechnology companies that offer the possibility of new paths for industrial production of novel drugs. This trend is turning drug development upside down. As opposed to chemical manufacturing, biotech takes a market-driven approach, looking at a specific cell and a particular disease, then developing a treatment for that. Manufacturing is a particular challenge in biotechnological processes. Production processes of large biological molecules are often difficult to scale-up. This is an area where the pharmaceutical industry's decades of large-scale manufacturing experience can support the development of biotechnological processes.

Modern biotechnology is typically a science-led technology, in the sense that most of the inventions, processes and product innovations have emerged from breakthroughs in scientific and technological research undertaken in universities, research institutes and industrial R&D departments. Those institutions also provide the professionals that will collaborate in the design and building of the industrial plants for the production of novel pharmaceutical products.

However, there is still a long way between the successful completion of small-scale manufacturing, and the concretion of industrial production plants. The traditional chemical industry relies on the support of a well-developed chemical engineering science. Chemical reactor design, and both upstream and downstream operation techniques are available in the expertise of well trained chemical engineers and even in computational codes that alleviate the task of equipment selection, sizing and design for an industrial process.

/// A growing number of chemical and especially pharmaceutical companies are taking deep interest in the industrial biotechnology field. ///

During the past two decades, the application of all these chemical engineering instruments for biochemical processes has been rapidly developing. To date, most of the academic institutes offer graduate degrees in biochemical and biotechnological engineering, which aim at integrating the inherent complexity of living organisms into classical process design techniques.

Yet, biological systems are exceedingly complex and defy the standard procedures. Very often a biological process becomes a special challenge (especially when the product is intended for pharmaceutical use), and at times requires unique and tailor made solutions. Below are a few examples:

The challenges may be in the reactor design, for example, in the manufacturing of a desired protein in photosynthetic cells. The design of photo bioreactors at the practical level is still carrided out following rough rules and trial and error. A relatively sophisticated model for photosynthetic growth considering the complex behavior of the system (photo-inhibition, photo-adaptation) has been recently published [1,2], but the correct design requires the integration of this mathematical model with the liquid flow dynamics in the bioreactor.

Another example is the growth of duckweed for the expression of aprotinin in lemna. Researchers from the Weizmann Institute have designed the conditions for the insertion of genes and the growth of lemna to obtain high protein production. From the process point of view, this is a unique system. The lemna is a free-floating, minuscule plant. In contrast to classic reactors, the biomass floats, forming a carpet-like film. The culture, while requiring a certain liquid volume for the provision of substrates, remains only on the surface. Such a system is quite far apart from classical chemical reactors, and requires a special process design method and a mathematical description of it, which still has to be developed [2,3].

In the third example, the uniqueness lies in the target. If the aim is the separation of an organelle and not of a molecule, the challenge is unique. StarletDerma, a recently created company develops and commercializes enhancer suspensions that accelerate epidermal delivery, and improve compliance with active ingredients in a wide range of applications [101]. The epidermal delivery platform is based on the natural, 700 million-year-old micro-injector mechanism found in sea anemones. The technology harnesses the natural mechanism of these micro-injectors, processes them into a gel that can be combined with commercial creams or sprays to accelerate and enhance their skin penetration [4]. No standard chemical engineering methods for the separation of organelles exist, and the adequate procedures for a large-scale production are to be specially designed and developed.

The three examples highlighted here clearly show that the engineering of pharmaceutical processes very often leads to problems that exceed the limits of usual chemical plant design,

and requires novel and sometimes unique solutions. This fact has to be taken into account in the education of professionals in the field of pharmaceutical engineering. A deep knowledge of modern biology and pharmacology must be balanced and integrated with the classic principles of mass, energy and momentum transfer in the education of new generations of pharmaceutical engineers. Creative analysis of problems should therefore be stressed and given extra weight in the teaching schemes of universities and colleges teaching engineering of biological processes, side-by-side with the learning of classic methods design and scale-up. The development and industrial-scale production of the next generation of novel bio-pharmaceutical products is a challenge we must be ready to meet.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

References

1 Merchuk JC, Garcia-Camacho F, Molina-Grima E. Photobioreactors. In: *Comprehensive Biotechnology*. Wiley, NY, USA, 144 (2010).

2 Garcia-Camacho F, Miron AS, Molina-Grima E, Camacho-Rubio F, Merchuk JC. A mechanistic model of photosynthesis in microalgae including photoacclimation dynamics. *J. Theor. Biol.* 304, 1–15 (2012).

3 Shaoul E, Ayalon A, Tal Y, Lotan T. Transdermal delivery of scopolamine by natural submicron injectors: *in vivo* study in pig. *PLoS ONE* 7(2), e31922 (2012).

4 Aviezer D, Brill-Almon E, Shaaltiel Y *et al*. A plant-derived recombinant human glucocerebrosidase enzyme – a preclinical and Phase I investigation. *PLoS ONE* 4(3), e4792 (2009).

» Website

101 StarletDerma. www.starletderma.com