Book review

Green chemistry strategies for drug discovery

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Further than a simple set of rules, green chemistry (GC) has become nowadays both a philosophy and fortunately a custom: thus, a new way of conceiving of environmentally friendly chemical processes beyond the final product. GC is one whole package composed of parts which cannot be separated from one another (lab development, process design, process operation, purification, analysis, …). This is on the way to be applied to all fields of biochemistry, pharma and chemical engineering through a holistic view from cradle to grave. This book, entitled *Green chemistry strategies for drug discovery* (edited by Emily A. Peterson and Julie B. Manley), gives a comprehensive overview of such philosophy, focusing on all steps from the birth of the idea up to the environmental impacts after its use, in an integrative approach. GC slowly becomes routine when new compounds are designed and synthesized from scratch. Its postulates and desire for ever better process improvement are nowadays often connected, providing an ecological view for the latter. Indeed, the reduction of the process time of work and the amount of reagents needed through process optimization, intensification and simplification will finally result in energy, time and space savings. This is widely taken up by companies, which protect such innovations through patents (chapter 12). However, nowadays it is not clear whether GC's success is because of a conscious inclusion of such values to the scientific community or it is just the consequence of what its application means for business in terms of economical savings (chapter 13). In any case, the GC, despite tackling economic, technical or even cultural hurdles (chapter 2), is being consolidated as a reference when developing holistic process designs, as it can be applied down the line (chapter 1).

Since the early 2000s, it has become easier to find in the art parameters such as *E-factor*, *process mass intensity* and *atom economy* in assessing the viability of a chemical process. In this context, the 21st century technology gives the scientists tools at hand that allow them to let their research be guided by the objectives of GC. One eminent asset here is that all chemicals are chosen in accordance to the directives and regulations, such as the European Registration Evaluation Authorization and Restriction of Chemical Substances (REACH) (chapter 11).

The following issues are crucial when considering the full life cycle of a chemical product: as an integral part of reaction design, solvents selection strategies and workup procedures are to be developed or improved (chapter 3). In this view, the process design *ex-ante* becomes more relevant as well as the previous *reaction screening* as described in chapter 5 or the computational design of chemicals (CDC). These procedures, also included in the GC postulates, avoid unnecessary tests and find bottlenecks leading finally to lower costs. Specifically concerning CDC (chapter 9), such technology is linked to the increasing capacity and performance of computers and the increasing access to databases through internet connections. The computer-aided design of a drug that includes a forecast of possible by-products, as well as of the drug properties and toxicity, is today a reality yet just a few years ago was regarded as a seemingly impossible challenge. As another asset in the overall green process and product analysis, toxicokinetics and toxicodynamics analysis (chapter 10) allow to predict all effects as well as environment and health outcomes.

On the production side, framed into good manufacturing practice (GMP), continuous flow chemistry is considered as one of the main challenging strategies (chapter 6). As a result, high control over product and by-product formation is achieved, enhancing the yield and reproducibility of the reactions, minimizing the need of solvents and hazards, and thus leading finally to an *E-factor* improvement. Under such conditions, new pathways can be achieved, including formerly hazardous chemistries which are done now under safe conditions. This effect can be enhanced by coupling to other advanced techniques such as microwave, electro-synthesis and photo-catalysis to micro-reactors. In addition, these capillary devices can be used with catalysts in the so-called packed-bed reactors, where heterogeneous catalysts are preferred according to the GC because of their easy recycling (chapter 8). Saving water is other interesting strategy in GMP,

especially in the field of bio-pharma (chapter 7), where the GC postulates are slightly amended in the way to reduce its consumption because of the risk of environmental contamination derived from industrial processes. Such problem can be circumvented by using techniques such as continuous perfusion chromatography in bioreactors, which uses 25% less buffer and requires 50% less water in purification. This is an example of how a holistic life cycle assessment can spotlight the parameter of highest impact.

In referring to the purification, the technological breakthroughs are to reduce the use of solvents to minimum while improving efficiency (chapter 4). In this context, new technologies such as supercritical fluid chromatography provide an alternative, which have potential for higher performance than HPLC and TLC procedures concerning time, resolution and low waste generation. It is also considered valuable to advance the latter current technologies. For example, there is a trend to operate HPLC columns with less amount of solvent or, as referred to in the book, to the development of procedures such as "in-column dilution".

Beyond drug production and GMP, there is a chance for exploiting GC postulates in the "very normal" operations of laboratories in the way of so-called Good Laboratory Practice (chapter 8). This comprises, among others, glass recycling, security or to use different bins for waste but, once more, to use less amount of solvents in the workup and also to take special care with the use of precious metals.

To sum up, the authors of the book provide a very useful and holistic overview of cutting-edge tools that we have at our fingertips to put these in place, to improve our production process or just to change our way of working in researching synthesis toward a greener perspective. The book succeeds in being a bridge between chemistry and sustainability GC postulates, suggesting strategies for both economic and environmental assessment in a multidisciplinary chemical approach.

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