EDITORIAL

All natural

Natural products research focuses on the chemical properties, biosynthesis and biological functions of secondary metabolites. As our scientific understanding of all things ‘natural’ is rapidly expanding, we should also make time to communicate the subtleties of chemical distinctions to the public.

Natural products are a central theme of research at the interface of chemistry and biology. The complex structures captivate the chemical thinking of scientists, both by offering countless opportunities to flex synthetic organic muscles and by engaging chemical intuition in thinking about how these molecules might have originated in the cell. Elucidating the relevant biochemical pathways and deciphering the roles of the compounds within a biological setting, on the other hand, pushes our understanding of small-molecule mechanisms in biology. Though all natural products have served to inspire intellectual inquiry, one of the most intriguing classes of molecules is the terpenes. These highly diverse and amply decorated scaffolds remind us that, amidst our growing chemical and biological understanding, open questions remain. Accordingly, the collection of articles in this special issue demonstrates that ongoing research on natural products, and terpenes in particular, is flourishing. But against this backdrop of significant scientific advances in understanding the chemistry and biology of naturally occurring small molecules, there is a need for increased public awareness of what it means to be ‘natural’.

In the public eye, products dubbed ‘natural’ and ‘organic’ are typically viewed as good and wholesome, whereas ‘chemicals’ have negative connotations. Beyond being a frequent source of amusement for scientists, and organic chemists in particular, this prevailing viewpoint has consequences. In the consumer market, it has manifested itself in one case as a lawsuit between companies producing ‘real’ sugar (http://pubs.acs.org/cen/news/85/i16/8516notw5.html). In the agricultural sector, there are significant public misconceptions about the potential dangers and benefits of genetically modified crops (http://www.nature.com/nature/focus/gm/index.html). The emerging field of synthetic biology faces a related challenge in maintaining open communication with the public about the risks and rewards of engineering organisms (http://www.nature.com/naturejournal/v438/n7067/edsumm/e051124-01.html), for instance, to produce small-molecule therapeutics.

But what is ‘natural’? The simplest definition for a natural product is a small molecule that is produced by a biological source. However, one challenge in classifying chemicals as natural or non-natural is the limited extent to which natural products have been characterized. As Fischbach and Clardy point out, many biosynthetic enzymes are non-specific, which results in the production of multiple ‘natural’ analogs (Commentary, p. 353). Similarly, the ongoing discovery of new microorganisms and the subsequent identification of the natural products they produce suggests, as Axel Brakhage, director of the Hans Knöll Institute puts it, that we’re “only at the tip of the iceberg” in identifying the entirety of natural products (Elements, p. 367). Indeed, new research in this issue reexamines the natural products that make up the dauer pheromone, finding two new compounds that account for the bulk of the biological response (Letters, p. 420; News & Views, p. 368). With so many compounds undiscovered, the definition of a natural small molecule is clearly a moving target.

In contrast, for cases in which the chemical structure of a small molecule has been determined, defining natural (for a scientist) becomes easy. Whether a natural product is isolated from a native organism, synthesized in a laboratory (Review, p. 396), biosynthesized in vitro, or isolated from a metabolically engineered organism (Perspective, p. 387), if the resultant compound is chemically equivalent to the original natural product, it is natural. In contrast, even if a molecule is produced by biosynthetically engineering a microbe (Perspective, p. 379), if it is not a naturally occurring small molecule, it is not natural. However, this type of engineering represents an important source of potential new therapeutics, and the existence of many natural product ‘analogs’ among currently used drugs (J. Nat. Prod. 66, 1022–1037, 2003) defies the simplistic public connection between natural and good.

Despite society’s association of ‘natural’ with wholesome products, we all know that natural products include toxins and poisons, and even compounds that are required for life at low concentrations can become dangerous at high concentrations. Gershenzon and Dudareva discuss some of the ways that natural products are used in defense (Review, p. 408), highlighting chemicals used by plants to poison herbivores directly and to protect the plant indirectly by attracting predators. Schmidt et al. tackle the question of how to make use of these and related plant-derived compounds. In a discussion of the challenges in regulating natural product concentrations in botanical extracts, they point out that lax or poorly defined regulations have eroded consumer confidence in these products, despite the ‘natural’ moniker (Commentary, p. 360).

The many uses of ‘natural’ and the subtle distinctions between some cases of natural and non-natural clearly leave room for debate. However, better communication between scientists and the public is the first step in putting public debates on scientific footing. Indeed, Strobel and Strobel have taken on one aspect of this challenge in an undergraduate educational program in which students collect and culture new microorganisms and then isolate and identify the natural products they produce (Commentary, p. 356). The practical research experience of these young scientists will cement their understanding of the definition and significance of natural products; imbuing the public with similar enthusiasm for chemical principles should be a community goal. With ideas like this as our guide, it’s time to move beyond advertising gimmicks and fearmongering as pseudoscientific slogans and progress into real scientific dialogue.