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LETTERS

Drugs from Third World Plants: The Future

I. S. Johnson (Letters, 14 Aug., p. 860) debunks persuasively the oversimplified, populist arguments why Eli Lilly & Co. owes millions in "royalties" to Madagascar for the exploitation of a common *Vinca* species in the development of the anticancer drugs vinblastine and vincristine. These naturally occurring alkaloids are historically instructive examples of medicinally important drugs, which, without further chemical transformation, continue to be obtained from plant sources. The future, however, of most new, medicinally useful drugs derived from the Third World or any other natural plant source is likely to be different.

Given present sophisticated isolation, separation, and especially structure elucidation techniques (for example, computer-aided mass spectrometry, nuclear magnetic resonance, and x-ray diffraction) as well as much more specific and material-saving screening procedures (for example, biological receptor technologies), the emphasis of most present medicinal research based on natural products is on the generation of *molecular leads* rather than final products. The synthetic chemist will either modify the original structure, thus coming up with a new drug, or else produce the natural product by synthesis. After a few hundred million dollars are spent to bring such a product to the regulatory approval stage, should royalties be paid to the Third World country where a few grams or even some kilograms of the original plant were collected? Or for a product originally derived from a marine organism collected within the frequently claimed (and disputed) 200-mile territorial limit of certain countries? Suppose the plant came from Switzerland? Should royalties be paid to a Swiss canton by a Lilly, Glaxo, or Ciba-Geigy? If we wish to contribute to the economic well-being of a Third World country—and I am all for it—let us do it on more logical grounds.

There is one instance where a real argument existed for financial reimbursement to a country for the exploitation of a wildly growing local plant—the isolation of diosgenin from Mexican *Dioscorea* species, which, starting in the late 1940s, led to a booming steroid industry in that country (*1*). By that time, the Mexican government had imposed prohibitively high export duties on the *Dioscorea* plant as well as on diosgenin, in order to stimulate the establishment of a local advanced steroid manufacturing industry performing the much more complex chemical steps whereby diosgenin was converted into higher value finished hormones, such as progesterone and testosterone, that were then exported. This enlightened step led to the training of a new generation of Mexican chemists; to the eventual establishment of Mexican industrial research laboratories [for example, Syntex, which *Fortune* (*2*) in 1951 termed "the biggest technological boom ever heard south of the border"]; and to a budding graduate chemistry program at the National University (UNAM)—a process (*1*) that within 10 years made Mexico the world's center in steroid hormone production, research, and patents. According to Harvard University's L. F. Fieser at a Gordon Research conference (*3*), more papers originating from Syntex in Mexico City were cited in his famous monograph (*4*) than from any other pharmaceutical company in the world.

One of the key factors in the collapse of these uniquely promising developments was precisely the type of naïve populist thinking reflected in recent pronouncements about "drugs from Third World plants." In the late 1960s, a different Mexican government decided to nationalize the plant collection and production of the cheap basic raw material, diosgenin, the base of the entire inverted pyramid of Mexican-produced hormones and synthetic steroids (oral contraceptives, topical corticosteroids, anabolics, and so forth), and to raise the price of diosgenin by several hundred percent. The ostensible argument was to bring more wealth to the poor peasants collecting the wild-growing yams, rather than to continue supporting the flourishing export business of advanced intermediates and final products by the affluent steroid manufacturers. This was chemical OPEC (Organization of Petroleum Exporting Countries) thinking with one fatal flaw (*5*): While it may take decades to come up with economically attractive alternatives to petroleum as an energy source, it took the international pharmaceutical companies only a few years to come up with other alternatives (total synthesis, use of other competitive steroid raw materials, and more extensive use of microbiological fermentation techniques) that transformed the Mexican di-

osgenin-based steroid industry into a minor player on the world stage—a transformation from which Mexico has never recovered.

As is so common in gray area problems of great complexity, where economic, political, and scientific factors as well as feedback mechanisms operate, oversimplified black and white solutions tend to prove counterproductive. The Mexican example shows that they can even lead to economic hara-kiri. Most of us want better new drugs, a more equitable distribution of the world's wealth, less dependence by three-quarters of the world on the technological prowess of the other quarter, and so forth. But naïve proposals and a refusal to learn from history will not accomplish those meritorious aims. *Caveat lector*!

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REFERENCES AND NOTES

1. For a recent personal view, see C. Djerassi, *The Pill, Pygmy Chimps, and Degas' Horse* (Basic Books, New York, 1992), chapters 4 and 5.
2. *Fortune*, May 1951, p. 87.
3. L. F. Fieser, reproduced in C. Djerassi, *Steroids*, in press.
4. _____ and M. Fieser, *Steroids* (Reinhold, New York, 1959).
5. C. Djerassi, *Proc. R. Soc. London Ser. B* **195**, 175 (1976).

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Space Station Freedom

Ivan Amato's article "Microgravity materials science strives to stay in orbit" (Research News, 14 Aug., p. 882) leaves a somewhat misleading impression regarding the ability of Space Station Freedom to support basic scientific research. Both of the reports cited by Amato (*1*) emphasize the need for a coordinated program of basic and applied research as well as the need for both manned space facilities (such as Space Station Freedom) and complementary unmanned facilities.

Space Station Freedom has been designed with the flexibility to be refitted in space over a 30-year period so as to accommodate a changing mix of research. This flexibility will allow both basic and applied research in a variety of disciplines to be done simultaneously. The foundation built by good basic research will progress to innovative commercial applications. Applied research is a follower, not a leader.

Amato cites the lack of access to space flight opportunities as hindering our understanding of basic phenomena. This is