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Cannot See the Flowers nor the Tree: Plants and the Pill

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The modern world suffers from a syndrome known as plant blindness—the inability to perceive plants.¹ The lack of awareness occurs in the natural environment, the home landscape, and even the scientific lab. The third article in the inaugural issue of the American Chemical Society's *ACS Central Science*² recognizes Carl Djerassi's pioneering work in steroidal syntheses. However, the article belies the essential role that plant natural products played in one of the most significant technological achievements of the 20th century.

The author the *ACS Central Science* article writes, "Scientists' first attempts to create birth control pills focused on extracting progesterone from plants and animals. However, this approach failed to yield an effective oral medication."² There are three major flaws with these statements. First, progesterone's insolubility in water and short half-life make it a poor candidate for oral contraceptives.³ Second, plants were not sources of progesterone, but rather sources of steroidal sapogenins that could be converted into progesterone and other steroids. Third, and the focus of this paper, Djerassi acknowledged the pioneering work of Russell Marker and the role plants played: "Marker ... made me focus on steroidal sapogenins [plant

natural products] as starting materials for the synthesis of estrone and estradiol—steroid hormones that had not been part of his synthetic repertoire."⁴

Marker had successfully produced progesterone from the sapogenins diosgenin and sarsasapogenin (Figure 1), but none of the known plant sources yielded sufficient quantities of sapogenins to be cost-effective for industry. The intrepid chemist then began a search for better sapogenin sources which led to a Mexican species of yam (*Dioscorea mexicana*). Pharmaceutical companies spurned his discoveries, so Marker moved to Mexico and started Syntex, S.A. in 1944. His involvement with Syntex was short, and, following a quarrel with his partners, he soon left the company. Syntex floundered without Marker's expertise and lab notes, until the company hired George Rosenkranz, who recruited Carl Djerassi and other talented chemists.⁵ After joining Syntex in 1949, Djerassi synthesized both cortisone and norethisterone, a progesterone mimic, from diosgenin extracted from *Dioscorea mexicana*.⁶

The role of plants in supplying the starting material for subsequent modifications is unquestioned and is noted by physicians, historians, and scientists, including Djerassi

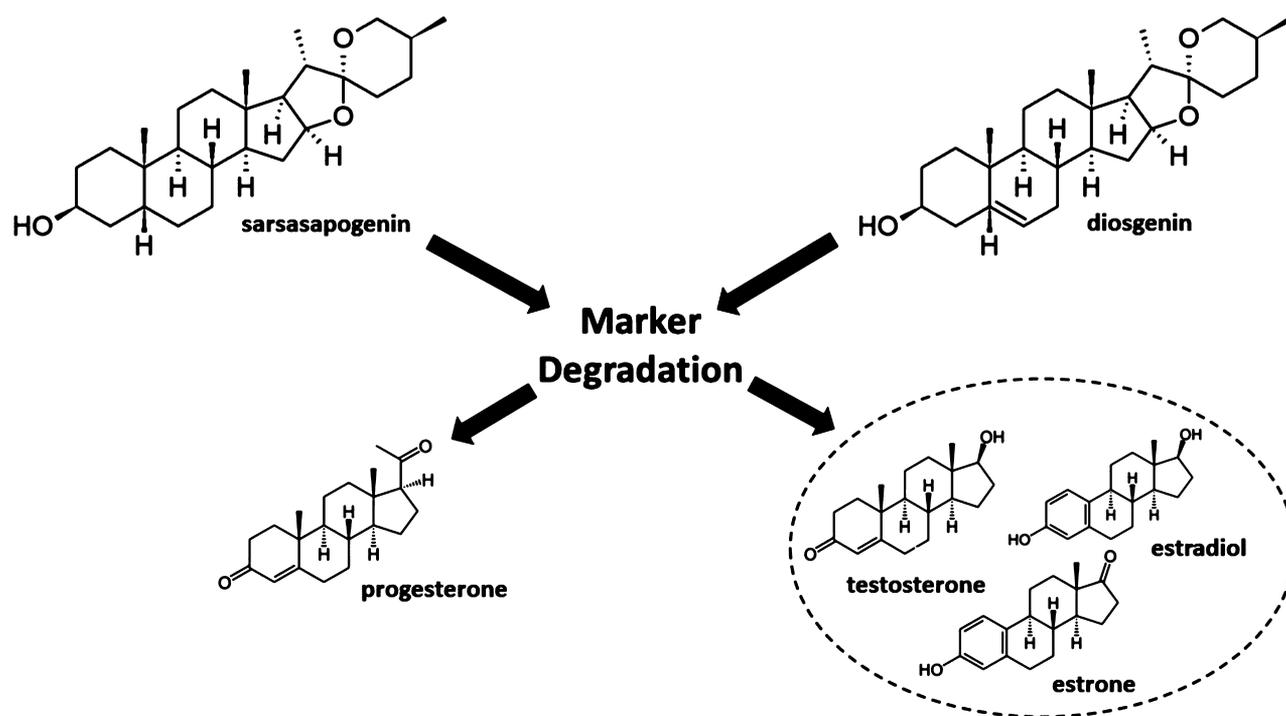


Figure 1. Marker degradation, which converts plant sapogenins into medically important steroids.

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himself: “Interestingly, this genesis of estrogens ... led us in a fairly straight path to the first synthesis of an oral contraceptive in the same year (1951) in which we also announced the first synthesis of cortisone from a plant raw material—at that time arguably the hottest problem in synthetic organic chemistry.”⁴

Plants continued to play a vital role in the steroid industry after the initial euphoria of the 1940s and early 1950s. Another plant steroidal saponin, hecogenin, was first discovered in the terrestrial bromeliad *Hechtia texensis* (Bromeliaceae). It also occurs in the cultivated species sisal (*Agave sisalana*, Asparagaceae), which is the source of the fiber of the same name. Syntex pioneered the production of cortisone from sisal-derived hecogenin.⁷ The Mexican company licensed the process to Glaxo, which developed top selling drugs, including betamethasone and beclomethasone.³ Both have been on the World Health Organization’s list of essential medicines, and many other drugs on the list are either plant derived or based on chemical structures first identified in the botanical kingdom (e.g., artemether, *Artemisia annua*; etoposide and teniposide, *Podophyllum peltatum*).

Chemists’ blindness toward plants stems from the term synthesis. When they describe the “synthesis” of a compound from or based on the structure of a natural product, they conceal the diversity of nature’s chemical palette and disregard the role of natural products. Plants continue to be the source of new lead compounds as well as new drugs. The work of many Nobel prize-winning chemists from Hermann Fischer’s sugar and purine syntheses (1902) to Elias Corey’s organic syntheses, including ginkgolides (1990), has been based, at least in part, on plant natural products. Let us not forget the importance of plants as sources of compounds for chemistry, medicine, and industry.

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Notes

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■ REFERENCES

- (1) Wandersee, J.; Schussler, E. Toward a theory of plant blindness. *Plant Sci. Bull.* **2001**, *47* (1), 2–9.
- (2) Berg, E. G. The chemistry of the pill. *ACS Cent. Sci.* **2015**, *1* (1), 5–7.
- (3) Mann, J. The birth of the pill. *Chem. World* **2010**, September, 56–60.
- (4) Djerassi, C. Chemical birth of the pill. *Am. J. Obstet. Gynecol.* **2006**, *194* (1), 290–298.
- (5) Anonymous. *The “Marker Degradation” and Creation of the Mexican Steroid Hormone Industry, 1938–1945; An International Historic Chemical Landmark*, University Park, Pennsylvania, October 1, 1999, and Mexico City, December 2, 1999; American Chemical Society and Sociedad Química De Mexico: 1999.
- (6) Ball, P. Carl Djerassi (1923–2015): Chemist, writer and contraceptive-pill pioneer. *Nature* **2015**, *519*, 34.
- (7) Davenport-Hines, R. P. T.; Slinn, J. *Glaxo: A History to 1962*; Cambridge University Press: Cambridge, U.K., 1992.