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The Lucius Sayre Legacy: Reviving the Study of Medicinal Plants of the Plains

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INTRODUCTION

The Native Medicinal Plant Research Program, a collaboration between University of Kansas labs at the Kansas Biological Survey (Kelly Kindscher's ethnobotany lab) and the Department of Medicinal Chemistry (Barbara Timmermann's natural products chemistry lab) has revived key components of the medicinal plant work of Lucius E. Sayre, the first dean of the KU School of Pharmacy. Sayre conducted research on numerous medicinal plant topics from 1885 until his death in 1925. During this time he wrote prolifically, including more than 180 articles, with more than 50 published in the Transactions of the Kansas Academy of Science. Sayre studied the medicinal chemistry of native Kansas plants and promoted the idea of medicinal gardens at schools of pharmacy. He also was deeply concerned about the safety and efficacy of medicinal plant use and conservation of medicinal plants, which continue to be important issues today in medicine and in the herbal products industry. In discussing his work, we want to emphasize to researchers the importance of previously published work in the Transactions and similar publications in regional and state academies of sciences. We believe this past scholarship can significantly benefit our scientific research today.

The KU Native Medicinal Plant Research Program

A central goal of the Native Medicinal Plant Research Program (2012) is to identify naturally occurring medicinal compounds in plants native to Kansas and the Great Plains. Much of the program's research echoes Sayre's by focusing on the chemical analysis of native plants traditionally used for medicinal purposes. Primary funding for the program comes from Heartland Plant Innovations Inc., one of the Kansas Bioscience Authority Centers of Innovation.

Under the direction of Kindscher, a senior scientist at the Kansas Biological Survey and a KU professor of environmental studies, and after two full seasons of fieldwork (2010 and 2011), a team of botanists, with the help of students from KU and from Haskell Indian Nations University, have collected more than 250 species. Plants are selected for testing based on historical uses by Native Americans and settlers, as recorded in ethnobotanical records, as well as leads identified through medicinal chemistry research, which includes Sayre's findings. We collect enough fresh plant material to result in 1 kg of dried plant material. We also catalog plant collection data, create an herbarium voucher, and separate and archive a small amount of material as a DNA sample. Under the direction of Barbara Timmermann, KU Distinguished Professor and chair of the Department of Medicinal Chemistry,

a team of chemists at the KU Natural Products Chemistry Laboratory extract and analyze the plants using state-of-the-art screening techniques, including cutting-edge high-throughput screens, to examine underexplored biota and identify bioactive compounds.

Previously gathered information from sixteen Great Plains Native American tribal groups (see Kindscher 1987, 1992), along with the work of leading ethnobotanists and the Native American database by Moerman (2012), guided the development of a list of medicinal plants to collect. Combining this information with research findings generated by the medicinal plant program, we created a Prairie Ethnobotany Database that houses information on the medicinal and edible use of selected plants. In addition, we looked for other sources of information to guide our work, and Sayre became one of our major sources.

Sayre's work provided insights into *Echinacea* research

During the 1980s, while conducting research on the ethnobotany of the narrowleaf purple coneflower, *Echinacea angustifolia*, Kindscher (1989) found a helpful account, published 100 years earlier, of a study of *Echinacea* root chemistry and harvest in Kansas. This article by Sayre, titled "*Echinacea* Roots" (1903) provided information and informative accounts of the chemistry and harvest of *Echinacea* in Kansas. Sayre (Figure 1) read his description of the 1902 wild harvest and market before the Academy on November 27, 1903.

Sayre's study of the market for *Echinacea angustifolia* root showed that, at only 25 cents per pound in 1897, this native Kansas plant generated little profit despite numerous accounts of its

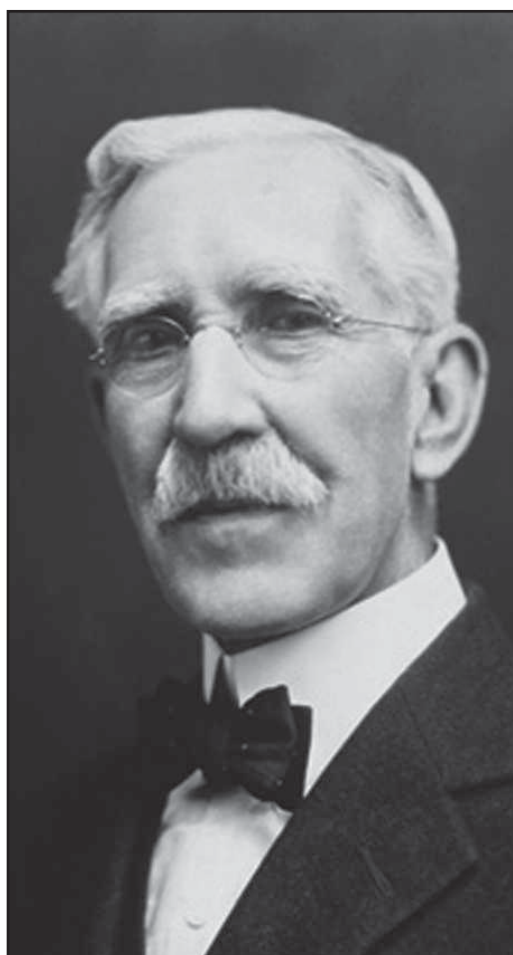


Figure 1: Lucius Sayre. University of Kansas Archives

medicinal efficacy as an antiseptic to treat a range of conditions including syphilis, wounds, diphtheria, typhoid, blood poisoning, and dysentery (Sayre 1897). By 1903 the demand for *Echinacea* had grown and its price doubled, which led Sayre to write to a U.S. Department of Agriculture official expressing his concern about potential overharvest (Sayre 1903). Fortunately, the demand for *Echinacea* soon declined, and wild stands had the opportunity to recover.

Sayre's body of published work on *Echinacea* helped provide background and historical information for other

research on *Echinacea angustifolia* in the Kindscher lab, including study of its population structure and the sustainability of wild harvest in Kansas (Price and Kindscher 2007; Price 1999). In 2012, *Echinacea* was listed as the sixth best-selling herbal product in the United States, grossing \$12.8 million (Blumenthal et al. 2011). Due to the market demand for *E. angustifolia* and the difficulty of cultivating it, this species makes up the majority of wild-harvested *Echinacea* for market (Price and Kindscher 2007; Kindscher, Price, and Castle 2008). As a consequence, concerns about overharvesting wild *Echinacea* in Kansas grew over the past century along with market demand (see Price and Kindscher 2007; Kindscher, Price, and Castle 2008). During the 1990s, more wild *E. angustifolia* was harvested in Kansas—perhaps millions of roots—than in any other state (Price and Kindscher 2007). Again there was concern about overharvest in the wild, in Kansas, but also in North Dakota and Montana. This led to funding for a study in which we conducted a conservation assessment for the U.S. Forest Service of wild harvested *Echinacea angustifolia* and other related species, especially *E. angustifolia* populations on National Grasslands and in National Forests in North Dakota and Montana, and on private lands in Kansas (Kindscher 2006). We concluded that wild harvest could be conducted sustainably but that other threats were of concern to the populations of *Echinacea*, including grazing and herbicide use, as well as conversion of *Echinacea* stands on private property to cropland, houses, and other land uses. And finally, we were able to publish data showing that within two years after harvest, about 50 percent of wild-harvested *E. angustifolia* plants re-sprout from their deep, tenacious root systems (Kindscher, Price, and Castle 2008). This unusual

characteristic supports the idea that wild harvest is mostly sustainable; it backs up the claims of those engaged in the wild harvest of Kansas *Echinacea* roots who have told us that “you can’t get rid of it” and that “it keeps coming back” after harvest.

Sayre and selection of medicinal plant species targeted for study

We discovered that Sayre had numerous published papers in the Transactions. Like the emphases of our medicinal plant research program, Sayre’s work centered on many medicinal plants, not just *Echinacea*, and was wide-ranging. It included chemical analysis of medicinally active plant compounds, a concern for the safety and efficacy of medicinal plant use, and significant contributions to the body of literature in the field of pharmacy. Among his books were the 1880 *Conspectus of Organic Materia Medica and Pharmacal Botany*; the 1894 *Essentials of Practice of Pharmacy*; and the 1900 *A Manual of Organic Materia Medica and Pharmacognosy*, still considered an important text today, and reprinted most recently in 2010 by Nabu Press, with Sayre still a co-author (Stevens and Sayre 2010).

But the two publications in the Transactions that influenced us the most were Sayre’s “*Therapeutical Notes and Description of Parts of Medicinal Plants Growing in Kansas*” (1897, read before the Kansas Academy of Science on October 28, 1897) and his two-part “*Cultivation of Medicinal Plants in the United States*” (1914, 1916). Several species Sayre mentioned have now been tested by our program, including *Echinacea angustifolia*, *Cucurbita foetidissima*, *Ipomoea leptophylla*, *Silphium laciniatum*, and *Solanum rostratum*.

Sayre's work also influenced Kindscher's collaborative work with other researchers, including Kirk Manfredi at the University of Northern Iowa, who requested that Kindscher collect prairie plants for medicinal chemistry analysis. In part because of Sayre's paper, *Cucurbita foetidissima*, and *Ipomea* (sic) *leptophylla* (1895), we collected bush morning-glory, *Ipomoea leptophylla*, from sandhills in western Kansas, and Manfredi's lab isolated an anti-tuberculosis resin glycoside from the roots of this plant (Barnes et al. 2003).

Research for the Native Medicinal Plant Research Program is beginning to bear fruit, too. The Timmermann lab has discovered new and interesting compounds in *Asclepias syriaca* (Araya et al., in press) and *Physalis longifolia* (Zhang et al., 2011). And some of the compounds in *Physalis longifolia* have significant anti-cancer activity.

Resurrecting Sayre's medicinal plant garden

Sayre's pragmatism and emphasis on the importance of giving students a strong foundation in the sources of medicine were manifest not only in his practical texts but also in his call for the establishment of a medicinal garden at KU. Sayre believed all schools of pharmacy should have medicinal gardens. For more than ten years, he petitioned the University of Kansas administration to allow him to establish a KU garden. He first appealed for local medicinal plant gardens in the wake of World War I to diminish American dependence on medicinal products manufactured in Europe (Sayre 1914). He believed medicinal plants should be, and profitably could be, grown in regions where they would thrive (Sayre 1914, 1916). Between 1914 and 1916, the profitability of medicinal plants soared, which gave

Sayre more reason to press the University for a medicinal plant garden at the School of Pharmacy (Sayre 1916).

In his call for a campus medicinal plant garden, Sayre was not necessarily ahead of his time—he makes reference to other such gardens at the universities of Minnesota, Montana, Nebraska, and Wisconsin, and at the University of the Sciences in Philadelphia (Sayre 1916)—but was remarkable in his fully developed vision of the potential educational and economic importance of native medicinal plants. It was not until 1927, two years after Sayre's death, that his goal of establishing a medicinal plant garden on campus was met. This garden, known as the KU Drug Garden, was planted on the south slope of the KU campus on Mount Oread, near old Robinson Gymnasium. Species included in the garden were listed in the caption of a photograph in the March 1927 issue of KU's Graduate Magazine, and this enabled us to identify species from a photograph found in the University Archives (Figure 2). We do not know how long this garden lasted, but academic priorities change, and at some point it was removed.

Barbara Timmermann held the same view as Sayre regarding the importance of students knowing the history of medicinal plant use and the origins of plant-based medicines. While she was being recruited to KU in 2005, though unaware of Sayre's early work, she spoke for the need of establishing a medicinal plant garden. The new KU School of Pharmacy provided an opportunity, and we were able to incorporate the garden into the landscape design. During the winter of 2010-2011, faculty and staff on the botany side of the medicinal plant program designed the garden and selected plant species for it.



Figure 2: KU School of Pharmacy Garden, 1927. Medicinal plants growing in the garden included: marshmallow, *Althaea officinalis*; absinth, *Artemisia absinthium*; cotton, *Gossypium hirsutum*; Job's tears, *Coix lacryma-jobi*; lambsquarters, *Chenopodium album*; rue, *Ruta graveolens*; foxglove, *Digitalis purpurea*; marijuana, *Cannabis sativa*; and poppies, *Papaver somnifera*. University of Kansas Archives.

In spring 2011, the Native Medicinal Plant Research Program, with the help of pharmacy students and other volunteers, planted the garden outside the newly constructed School of Pharmacy building at KU. In homage to the first KU Drug Garden, inspired by Sayre, the new KU School of Pharmacy Medicinal Plant Garden includes a bed with most of the same species grown in 1927.

The pharmacy medicinal garden (Figure 3) is about 300 square feet and made up of five different themed garden beds holding 60 species. The garden has extensive informational signage, making it a valuable resource for students as well as the public. Visitors are encouraged to smell and even taste certain plants, as indicated on the signage (other species, considered poisonous to eat, also are noted). The beds include: one holding all nine species

in the genus *Echinacea*; one made up of plants in the genus *Asclepias* (milkweeds); one made up of selected plants that have been part of the U.S. Pharmacopeia and National Formulary; a bed of medicinal tea and scented plants; and the Sayre bed of plants from the KU Drug Garden. The Sayre bed includes such species as marshmallow, *Althaea officinalis*; absinth, *Artemisia absinthium*; cotton, *Gossypium hirsutum*; Job's tears, *Coix lacryma-jobi*; lambsquarters, *Chenopodium album*; rue, *Ruta graveolens*; and foxglove, *Digitalis purpurea*. Two species—marijuana, *Cannabis sativa*, and poppies, *Papaver somnifera*—have been left out. Though they were important enough in Sayre's time to be included in the Drug Garden, we were concerned that these species' inclusion could pose legal issues or that they might disappear in the wee hours of the night.



Figure 3: KU School of Pharmacy Garden 2011. Kansas Biological Survey.

The gardens installed by the Native Medicinal Plant Research Program represent a strong connection with Sayre's work. Though only one element of an extensive program that includes wide-ranging research activities, this garden, in addition to a research garden we developed on agricultural land north of Lawrence, may constitute the most visible part of our work. Both gardens were planted during public events and are open to the public, and regular tours are held at the research garden.

Lucius Sayre's work has served as an important source of information and inspiration for our research and gardens. We believe that much of the research published in the deep archive of the Transactions, now available electronically, is still useful and relevant for research today.

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