

## Director's Message

April 9, 2024

### Advancing Research on Botanicals and Other Natural Products

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Americans spend about \$60 billion a year on dietary supplements. Many of these products contain plant-based or “botanical” ingredients and other natural products. These supplements are challenging to study because they are inherently variable and chemically complex. ODS partnered with the National Center for Complementary and Integrative Health (NCCIH) in 1999 to develop the NIH Consortium for Advancing Research on Botanical and Other Natural Products (CARBON) Program to help advance our understanding of the health effects of botanical dietary supplements.



The Botanical Dietary Supplement Research Centers were the first projects supported by CARBON. These centers focused on both characterizing the complex and variable chemistry of botanical dietary supplements and understanding their effects on human health. For example, clinical research in women conducted by the botanical center at the University of Illinois at Chicago investigated whether extracts of red clover and hops interact with medications. In the *Journal of Agricultural and Food Chemistry*, the researchers report finding no clinically relevant interactions between the [red clover extract](#) or the [hops extract](#) and commonly used medications. This is important information because these extracts are often used by perimenopausal and postmenopausal women who may also be taking medications.

Through its support of new botanical centers, CARBON has kept the dual focus on both characterizing botanical dietary supplements and evaluating their health effects. As each center adds new knowledge, we enhance our ability to design randomized controlled trials (RCTs)—the gold standard of clinical research for understanding the biological effects of a product. For example, the [Botanicals Enhancing Neurological and Functional Resilience in Aging \(BENFRA\)](#) Center established in 2020 has been studying extracts of *Centella asiatica*, a botanical commonly known as gotu kola that is often promoted for brain and nervous system support. To work toward a highly informative RCT of centella, the BENFRA researchers are trying to better understand centella chemistry as it relates to potential health effects and identify the best outcomes to study in an RCT. In a 2023 study published in *Nutrients*, BENFRA researchers examined fruit fly behaviors commonly inhibited by stress—sweet-seeking and climbing—and discovered that two related chemical constituents of centella, called caffeoylquinic acids (CQAs), enhance resilience to stress. They also discovered that a different group of compounds, called triterpenes—which are commonly used to standardize commercial centella products—had smaller effects than the CQAs on these behaviors. The knowledge gained by the BENFRA investigators will inform future RCTs to determine whether centella extracts can help protect people from the adverse effects of stress.

The [Center for High Content Functional Annotation of Natural Products \(HiFAN\)](#) has taken a technological approach to identify and connect chemical constituents of botanical dietary supplements with biological activities. A suite of online tools available on the HiFAN website helps researchers determine the chemical identities of compounds in botanical dietary supplements and simultaneously pinpoint which of those compounds may have important biological activities, such as immune or nervous system effects. These tools save valuable time compared with obtaining pure samples of chemical constituents and testing them individually to evaluate their biological activities. The tools also allow

researchers to detect when more than one constituent of an extract is required to elicit a given biological activity.

To build upon these and other research projects supported by CARBON, I am pleased to announce the release of three new [CARBON funding opportunities](#) in partnership with NCCIH and the National Institute on Drug Abuse. These funding opportunities will continue to advance our understanding of the mechanisms of action, bioavailability, and optimal product chemistry of promising botanical dietary supplements. Most importantly, they will identify objective outcomes relevant to studying human health. They will also support the expansion of a nuclear magnetic resonance database for natural products and the development of computational tools to help scientists use the database and drive natural product research forward.

To learn more about the CARBON Program and the recent funding opportunities, visit the [CARBON Program webpage](#) on the ODS website.



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