

## Botanicals and cardiometabolic risk: positioning science to address the hype

William T. Cefalu, Phillip J. Brantley

*NIH Center for the Study of Botanicals and Metabolic Syndrome, Pennington Biomedical Research Center,  
Louisiana State University System, Baton Rouge, LA 70808, USA*

Metabolic syndrome describes the human condition characterized by the presence of coexisting traditional risk factors for cardiovascular disease such as hypertension, dyslipidemia, glucose intolerance, and obesity, in addition to nontraditional cardiovascular risk factors such as inflammatory processes and abnormalities of the blood coagulation system. Although the specific etiology for metabolic syndrome is not known, insulin resistance—a clinical state in which a normal or elevated insulin level reflects an impaired biologic response—is present and is considered a key pathophysiological abnormality. As such, metabolic syndrome can be considered to be a prediabetic state and contributes greatly to increased morbidity and mortality in humans. As the prevalence is now reaching epidemic proportions worldwide, metabolic syndrome represents one of the most important public health problems facing our society today; and successful strategies are direly needed to intervene in its development. Although it is well established that caloric restriction and exercise greatly improve insulin resistance, the success of lifestyle intervention in humans over a long-term period is poor. Therefore, strategies to improve insulin resistance and components of the metabolic syndrome by pharmacologic approaches have remained as a major focus for drug development and are a primary and extremely viable option in clinical medicine. Unfortunately, recent data have questioned the safety of the current pharmacologic approaches to improve insulin resistance [1]. In this regard, alternative strategies, for example, nutritional supplementation with over-the-counter botanical agents, are extensively practiced by a large number of individuals with chronic diseases and are frequently undertaken without first informing the medical provider. However, considerable controversy has existed regarding the routine

use of most supplements on human health. In part, the controversy stems from the paucity of scientifically controlled clinical studies that have evaluated the effectiveness of any individual bioactive. In addition, the precise cellular mechanism of action for most botanicals has not been elucidated.

In an effort to address the above concerns, in 1999, the Office of Dietary Supplements (ODS) and the National Center for Complementary and Alternative Medicine (NCCAM) at the National Institutes of Health (NIH) collaborated in the development and funding of a botanical research initiative with major research institutions in the United States [2]. The Botanical Research Centers Program (BRCP) is the most visible activity of the initiative; and the program is intended to advance the spectrum of botanical research activities ranging from plant identification to early-phase clinical studies, with preclinical research encouraged as the primary focus of center activities [2]. Currently, the NIH funds 6 Dietary Supplement Research Centers focused on botanicals [2,3]. Each center has a thematic focus with high potential for being translated into benefits for human health. At the 2007 Experimental Biology Annual Meeting, the investigators from all 6 centers presented a workshop sharing research strategies used by the BRCP scientists and described approaches for testing the efficacy and safety of botanicals, particularly those used in dietary supplements. The entire body of that work summarizing the workshop was recently published [4].

As it relates to the studies reported for this special supplement, the theme for the Botanical Research Center that represents collaboration between the Pennington Biomedical Research Center of the Louisiana State University System, and the Biotech Center at Rutgers University is “Botanicals and Metabolic Syndrome.” The overall goal of our center is to provide a comprehensive evaluation of botanicals in addressing the pathophysiologic

---

E-mail address: [william.cefulu@pbrc.edu](mailto:william.cefulu@pbrc.edu) (W.T. Cefalu).

mechanisms that lead to the development of insulin resistance and the metabolic syndrome. Attainment of our goal will not only allow for specific investigation into the underlying mechanisms of this condition, but will provide the necessary data for future clinical trials for botanicals designed to intervene in the process. Thus, the articles in this supplement result from work supported by the NIH BRCP and range from overviews of botanical preparation and appropriate animal models for study of botanicals to specific studies by which botanicals may enhance cellular mechanisms of insulin action.

One of the more exciting lines of investigation featured in this supplement is the role that botanicals may play in epigenetics. *Epigenetics* refers to heritable changes in gene expression that are not attributable to changes in DNA sequence and impacts many areas of applied and basic biology. Epigenetic changes are known to contribute to aging in addition to multiple disease states; and epigenetic defects are thought to be more easily reversible (when compared with genetic defects) and, as such, have inspired efforts to identify novel compounds that correct epimutations or prevent progression to the disease state. Thus, it is exciting that a manuscript published in this supplement appears to be one of the first to report that botanical sources may be a rich source of agents that can potentially modulate the epigenome and related pathways and can potentially be useful in attenuating the progression of many factors related to the development of metabolic syndrome.

This special supplement of *Metabolism* would not have been possible without the funding of the BRCP by the NIH. Clearly, the time has come to provide the required science to either support a botanical for use in human health based on its effectiveness or to discourage use of a specific botanical based on no effect or even adverse effects. We hope you enjoy reading this supplement because the articles reported represent the rigorous and careful science needed for the study of botanicals.

#### Acknowledgment/Conflict of Interest

Supported by NIH Grant P50AT002776-01 from the National Center for Complementary and Alternative Medicine (NCCAM) and the Office of Dietary Supplements (ODS), which funds the Botanical Research Center of Pennington Biomedical Research Center and The Biotech Center of Rutgers University.

#### References

- [1] Nissen SE, Wolski K. Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. *N Engl J Med* 2007;356:2457-71.
- [2] Swanson CA, Liu QY. Introduction to the national institutes of health botanical research centers program. *Am J Clin Nutr* 2008;87:471S.
- [3] [http://dietary-supplements.info.nih.gov/Research/Dietary\\_Supplement\\_Research\\_Centers.aspx](http://dietary-supplements.info.nih.gov/Research/Dietary_Supplement_Research_Centers.aspx).
- [4] The science of botanical supplements for human health: A view from the NIH Botanical Research Centers. *AJCN* 2008;87(Suppl):465S-513S.