

Therapeutically promising new findings for combating hypertension and cardiovascular disease

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More than one-third of the world's population suffers from hypertension (commonly known as high blood pressure) and cardiovascular disease (disorders that affect the heart and/or blood vessels). The U.S. Agency for Healthcare Quality and Research has reported that Americans spent \$29 billion for non-prescription cardiovascular drugs alone in 2008. With the number of individuals afflicted on the rise, and the costs for treatment on the increase, scientists and policymakers are looking for new approaches to combat these disorders.

A team of Wisconsin and Texas scientific researchers have discovered a promising new avenue they strongly believe can be further developed to treat the diseases. The researchers are Md Abdul Hye Khan, William B. Campbell and John D. Imig of the Medical College of Wisconsin, Milwaukee, and Vijaya L. Manthati, Jawahar L. Jat, and John R. Falck of the University of Texas Southwestern Medical Center, Dallas.

Drs. Khan and Imig will discuss the team's findings based on their research paper, "Novel Epoxyeicosatrienoic Acid Analogs Increase Sodium Excretion and Lower [Blood Pressure](#) in Hypertension," at the 2011 Experimental Biology meeting (EB 2011), being held April 9-13, 2011 at the Washington, DC Convention Center.

Two EET Analogs Found to Lower Blood Pressure, Reduce Kidney Injury

Key to the research is the role of endothelial cells, which line the narrow spaces of the body such as those inside the blood vessels and the heart. [Endothelial cells](#) produce arachidonic acid metabolites, a class of [fatty acids](#) that have biological actions that are beneficial for cardiovascular health. This production occurs through three primary enzymatic pathways. Two of these pathways, the cyclooxygenase and the lipoxygenase pathways, have been successfully targeted for the treatment of inflammation, pain, fever, and asthma.

The third enzymatic pathway is the cytochrome P450 pathway that produces epoxyeicosatrienoic acids (EETs) as major biologically active metabolites. EETs are endothelial-derived factors that significantly influence cardiovascular function. They can dilate blood vessels, lower blood pressure and have additional biologic actions including anti-inflammatory and anti-platelet aggregator activity. These biological activities have made EETs a very attractive therapeutic target for cardiovascular diseases.

For the last several years the research team has developed and synthesized an array of EET analogs, or chemical compounds that act as EETs. The EET analogs have been tested for beneficial cardiovascular actions. For this research study 35 different EET analogs were screened for their ability to dilate blood vessels. The screening produced five EET analogs that would be further examined to determine their ability to lower blood pressure in animal models of hypertension. Two of the five EET analogs administered to hypertensive animals effectively lowered blood pressure and reduced kidney injury.

Next Steps

According to Dr. Imig, "This work is a major step forward in obtaining our goal to develop novel EET analogs for the treatment of

cardiovascular disease." He added, "We strongly believe that these EET analogs are therapeutically promising and can be further developed as a novel treatment for hypertension and cardiovascular disease."

The next steps, according to Dr. Imig, are to test the EET analogs in other cardiovascular diseases and improve EET analog formulation for potential future use in humans.

Provided by Federation of American Societies for Experimental Biology

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