

**U.S. Food and Drug Administration/National Center for Toxicological
Research (NCTR):
Effects of Dietary Supplements in Aging Individuals**

This research project is designed to investigate the possible toxic effects of the consumption of large doses of the over-the-counter dietary supplements glucosamine and chondroitin sulfate on the metabolism of sugar by aging individuals who may have Type II diabetes. The project will also evaluate the effects that glucosamine or glucosamine and chondroitin sulfate in combination have on blood glucose, insulin, cholesterol, and triglycerides. Organ systems that will be investigated include liver, kidney, and eyes.

Lead Agency:

U.S. Department of Health and Human Services, U.S. Food and Drug Administration, National Center for Toxicological Research (NCTR)

Agency Mission:

The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation. The FDA is also responsible for advancing the public health by helping to speed innovations that make medicines and foods more effective, safer, and more affordable; and helping the public get the accurate, science-based information they need to use medicines and foods to improve their health.

Principal Investigator:

Julian Leakey, Ph.D.
Research Biologist
50 RM647 HFT-030
3900 NCTR Road
Jefferson, AR 72079

Partner Agencies:

National Toxicology Program (NIEHS)

General Description:

This research project is designed to investigate the chronic effects of the long-term use of glucosamine and chondroitin sulfate, over-the-counter dietary supplements commonly used for inflammation and chronic joint pain relief, and the possible interference of sugar metabolism in individuals who may have Type II diabetes. Approximately 40 million Americans have been reported to suffer from osteoarthritis; annual retail sales of these dietary supplements approached \$750,000,000 in 2004. Use of these dietary supplements

continues to increase among an aging US population that seeks to maintain hip, knee, and spinal health and, therefore, preserve mobility and productive activity.

Data indicate that the subpopulation of consumers using these compounds for chronic joint or arthritic pain management is in its 50's or beyond, are usually overweight, and may consume doses in excess of manufacturer's recommended levels. It is thought that the compounds in question could accelerate the development of vascular degeneration and other physiological and clinical effects associated with Type II diabetes. The potential for kidney degeneration may also prove to be an increased risk for Type II diabetes when these drugs are used for extended periods of time. The primary concern is for the individuals in this sub-group who are not aware they are Type II diabetics. The lack of dietary control has been shown to be a contributing factor in the development of this disease. Joint pain is increased as the level of obesity rises, which tends to cause these self-medicated individuals to routinely increase the dose of dietary supplements to offset the discomfort. When one considers that most of this treatment is without the knowledge or advice of a medical professional, these individuals could be endangering their future health to the point of loss of limbs, blindness, vascular disease, or even death. The data from this project will provide much needed information for the education of this aging population.

Excellence: What makes this project exceptional?

While use of the dietary supplements, glucosamine and chondroitin sulfate, continues to increase in the aging US population, there is currently no long-term toxicology data on these compounds. The depth and breadth of this study will provide insight as to whether glucosamine or glucosamine and chondroitin sulfate in combination, dosed at various concentrations, will have a lasting effect on organ systems that are also affected by diabetes. Of particular interest is investigating whether these dietary supplements can cause kidney damage in normal or diabetic animal models. The use of lean (normal) and diabetic (obese) rat models in this study act as surrogates of two human populations of individuals. The models will allow a comparison of the effects of these drugs under both physiological conditions and whether these supplements will cause kidney damage in either or both rat strains. The obese, diabetic rat begins to develop kidney sclerosis at 20 weeks of age; osteoarthritis also begins to develop at an early age in the obese rat. We therefore have a model that develops signs of disease at an early age, and a normal animal to which we can compare that disease development.

Significance: How is this research relevant to older persons, populations and/or an aging society?

Data indicate that the likely consumers of these readily available, over-the-counter dietary supplements, who use these compounds for chronic joint or arthritic pain management, comprise a large segment of the aging US population. Frequently these individuals are overweight and likely candidates for development of Type II diabetes. It is further thought that these supplements have the potential to accelerate the development

of vascular degeneration, kidney degeneration, and other physiological and clinical effects known to be associated with Type II diabetes.

Effectiveness: What is the impact and/or application of this research to older persons?

Glucosamine or glucosamine and chondroitin sulfate in combination are dietary supplements promoted and purchased to relieve the symptoms of chronic inflammation and joint pain. Consumers are predominately the middle-aged or older segment of our population; many are obese and at risk for the development of Type II diabetes. Significant numbers of these individuals self-medicate independent of medical supervision, to routinely increase the dosage to offset increased discomfort. There are currently no data to guide individuals on short- or long-term use of these dietary supplements. The data from this project will provide much needed information for the education of this aging population.

Innovativeness: Why is this research exciting and newsworthy?

As our population ages and becomes limited in mobility and productive activity, dietary supplements that are promoted to alleviate the pain and discomfort of inflammation, joint pain, and arthritis are used with greater frequency and at higher doses. Sound guidelines for use and appropriate dosages do not exist. As life expectancy of aging populations in the US increase, the potential for long-term use of glucosamine or glucosamine and chondroitin sulfate in combination also increases. Currently, there is no toxicology data on the effects of these drugs on multiple organ systems or on the potential for associated diabetes risk among aging, obese populations. This study promises to provide sound scientific data for such risk assessment.