Foul-smelling gas shows health benefits in reducing joint swelling

April 29 2013

A gas associated with the smell of rotten eggs has proven to effectively reduce joint swelling, in research which could lead to advances in the treatment of arthritis.

Scientists at the University of Exeter Medical School have discovered that a novel drug molecule, which slowly generates the gas hydrogen sulfide (H2S), effectively reduces swelling and inflammation in arthritic joints.

For years, H2S has been regarded as a highly poisonous by-product which is corrosive, flammable and explosive. But research is now showing an altogether more benign side to the substance.

Professor Matt Whiteman, of the University of Exeter Medical School, said the research, which is published online in the *Journal of Cellular and Molecular Medicine*, could pave the way for more effective treatments of arthritis and other inflammatory conditions. Prof Whiteman said: "H2S is widely dismissed as a toxic and foul-smelling environmental pollutant, but it has recently been shown to be created in humans and animals by a specific set of enzymes. Why would the body do this if it had no benefit? Our research has shown that the key to unlocking the therapeutic qualities of H2S is through slow release, mimicking the body's own production."

The team has previously shown that H2S levels were increased by up to four times in the knee joints of patients with joint diseases such as

rheumatoid arthritis, but intriguingly the higher H2S levels strongly correlated with a lower number of inflammatory cells in the joint. The latest study provides further evidence that the real role for H2S may be to combat inflammation, swelling and joint destruction.

Prof Whiteman added: "A patient will usually visit their doctor with a joint already inflamed, swollen and painful. Since the compound worked after arthritis was established, it may be useful in treating arthritis in the future. Many compounds can prevent arthritis in the laboratory, but of course nobody knows when they will get arthritis. Having a class of compounds which reduce inflammation and swelling when arthritis is already active is extremely exciting. These molecules may also be useful in other inflammatory conditions, and even in the inflammatory aspects of diabetes and obesity."

The study was part of a large collaboration funded by the Wellcome Trust and Arthritis Research UK, involving Professor Philip K Moore and Dr Julie Keeble from King's College London, as well as researchers at the National University of Singapore and Queen's University, Belfast. The team used primary human cells as well as a model of arthritis. Rheumatoid arthritis causes some cells to proliferate too quickly in the joint and secrete substances which promote tissue inflammation, swelling and eventually joint destruction. However, the H2S donor molecule prevented this secretion, and inhibited the activity of several enzymes which cause inflation. In the arthritis model, the compound did not prevent arthritis, but was highly effective at reducing joint inflammation and swelling once arthritis was established, suggesting H2S-based compounds may one day be useful in clinic.

The same team has previously found that people who are overweight or have diabetes have lower levels of H2S in their bodies than healthy adults resulting in higher blood pressure, poorer insulin sensitivity and higher levels of sugar in their blood. It has also been reported to promote

ulcer healing and reduce lung injury in smokers.

Co-author Dr Mark E Wood, at the University of Exeter, added: "Despite its reputation for being hazardous, H2S could in fact hold the key to solving some of the widespread health problems affecting the country. Our work is a major step in proving that it can be more hero than villain to the human body, providing it is administered in the right way, at the right time. We currently have several more efficient H2S donor molecules being evaluated with collaborators and this is a very exciting time for us."

Dr Julie Keeble, co-author from King's College London, commented: "The finding that H2S is able to reduce joint inflammation in experimental models makes it a very exciting prospect for treating arthritis. Many patients with arthritis do not respond effectively to current treatments or suffer side-effects from their medication. We hope that H2S-releasing drugs like the one tested in this study will be effective in treating arthritis without uncomfortable side effects."

Provided by University of Exeter