

The verdict on oxygen free radicals: Innocent!

A new study in Nature suggests 30 years of research costing billions has been "fundamentally flawed"

BY TONY CRAIG

Decades of research and hundreds of millions of dollars have been wasted chasing the red herring of free radicals' role in disease, according to British scientists. And if they're right, beliefs about why some vitamins are good may also have to be jettisoned.

Oxygen free radicals, the sinister little atoms and molecules accused of causing diseases ranging from cancer to arthritis to arteritis, may not actually be causing any diseases at all.

In fact, according to a team from University College London (UCL), medicine has been barking up the wrong tree on this issue for 30 years. They said that medication based on antioxidants -- a major focus of drug research for decades -- are being developed on the basis of a fundamentally flawed theory.

Instead, the scientists suggested, we need to look at treatments regulating enzymes released from neutrophil leukocytes, the most numerous of the white blood cells.

"White blood cells produce oxygen free radicals, and the process by which they do so is essential for the efficient killing of microbes," said Dr Tony Segal of the Centre for Molecular Medicine within UCL's Department of Medicine, one of the authors of the research. But people in whom this process is defective are prone to severe, chronic and often fatal infections. This fact has led to the presumption that the oxygen free radicals themselves are highly toxic and that if they can kill organisms as tough as bacteria and fungi they can also damage human tissues. Free radicals are believed to be promoted by many agents, including smoking and atmospheric pollutants, and have been implicated in the production of conditions such as cancer, and many others caused by an initial inflammation in which these neutrophil leukocytes accumulate.

"However," said Dr Segal, "our work shows that the basic theory underlying the toxicity of oxygen radicals is flawed. Tens, if not hundreds, of millions of

pounds have been misspent by the pharmaceutical industry in chasing the red herring of the involvement of oxygen free radicals in the causation of many diseases. Many patients might be using expensive antioxidant drugs based on completely invalid theories as to their therapeutic potential," he added. "All the theories relating to their causation of disease by oxygen free radicals, and the therapeutic value of antioxidants must, at the very least, be re-evaluated".

Many vitamins, notably vitamin E and C, as well as other natural substances are regarded as healthy because they attack free radicals. In reality, said Segal, free radicals aren't the agents of destruction when white blood cells attack foreign particles. They found that mice whose white blood cells were altered to be deficient in enzymes called neutrophil-granule proteases, but were able to produce free radicals as usual, were unable to resist staphylococcal and candidal infections.

They discovered that neutrophil-granule proteases are the real agents of destruction in the white blood cells' antibacterial arsenal. Production of these enzymes is triggered by the flow of potassium within the cell. When this flow was blocked, using a chemical derived from scorpion venom, the cells were unable to kill off foreign invaders.

If it's indeed the proteases and not the oxygen free radicals that are responsible for the destruction of bacteria, this removes the main basis for the assumption that free radicals are highly toxic. It also knocks out the theoretical underpinning behind a great deal of drug research, especially in cancer and autoimmune diseases. The research is published in the February 26 issue of the journal *Nature*.