

New effective treatment for inflammatory diseases found

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New research conducted by the University of Liverpool and AKL Research and Development Ltd (AKLRD), published in *Inflammopharmacology*, highlights the potential benefits of a new drug treatment on the human body's immune response in inflammation.

In a number of inflammatory conditions, such as osteoarthritis, [rheumatoid arthritis](#) and, more recently, COVID-19, major complications and extensive tissue damage can occur when the immune system becomes excessively and uncontrollably activated. Finding new ways to selectively control this over-activity could have major clinical benefits.

Neutrophils

To be healthy, we need an effective immune response, otherwise we would succumb to overwhelming infection, even by everyday bacteria. However, sometimes our immune system can become hyperactive and cause damage through inflammation, even in the absence of any infection. This can sometimes be extreme. Indeed, many [rheumatic diseases](#) such as rheumatoid arthritis and osteoarthritis are caused by inflammation. The quest has always been to find ways to selectively block the harmful effects of an overactive immune system, without paying the price of blocking our ability to fight infections.

Neutrophils are the most abundant immune cells in our blood. They are rapidly dispatched to sites of infection, where they fulfil their life-saving antimicrobial functions by destroying infectious organisms and producing signalling proteins called cytokines, that help co-ordinate the recruitment and activity of other [immune system](#) cells to the battle against the infection. There is much evidence from work in Liverpool to show that these cells are important players behind many rheumatic diseases

Cytokine storms and COVID-19

In some situations, if the levels of cytokines are too high, they can trigger an extreme inflammatory reaction called a cytokine storm. These

storms cause overwhelming inflammation that leads to blocked or ruptured blood vessels. This can affect the entire circulatory system. Cytokine storms can cause immense damage, multiple organ failure, sepsis, and even death and, appear to play a major role in severe COVID-19 disease.

For many decades scientists and clinicians have understood the potential benefit of suppressing neutrophils, but any attempt to do this without weakening the immune response to infection has failed.

APPA

APPA is a novel drug under development by AKLRD for use in osteoarthritis, a major disabling problem world-wide that is caused by low grade inflammation. The first part of its formal clinical evaluation in Liverpool, led by rheumatologist Professor Robert Moots, has recently been successfully completed. Now, in partnership between Liverpool and AKLRD, the impact of the drug on neutrophils has been examined and published.

The study found that APPA clearly demonstrated anti-inflammatory potential but without weakening host defence to [infection](#).

Robert Moots, Professor of Rheumatology at the University of Liverpool and Director for Research and Development at Aintree University Hospital, said: "We have shown that APPA has the potential to dampen down that bad inflammation that causes rheumatic diseases—but not impact on the crucial antimicrobial function of neutrophils. We have been waiting for too many years for such a selective drug."

"Our results suggest a prime role for APPA in helping safely modify aggressive [immune response](#), not only in the arthritis that I treat every day, but even, potentially, in COVID-19."

Professor Steve Edwards, a neutrophil scientist on the project at University of Liverpool said: "Therapeutically targeting the harmful effects of neutrophils in inflammation, without interfering with their ability to fight off infections, has been a long-term goal of many scientists worldwide. At last, we may be able now to realise this goal."

David Miles, CEO of AKLRD said: "These exciting results underpin the favourable clinical results observed in patients with Osteoarthritis, whilst also suggesting APPA has an important role to play in treating a broad range of conditions where [inflammation](#) is involved."

More information: A. L. Cross et al. APPA (apocynin and paeonol) modulates pathological aspects of human neutrophil function, without suppressing antimicrobial ability, and inhibits TNF α expression and signalling, *Inflammopharmacology* (2020). [DOI: 10.1007/s10787-020-00715-5](#)

Provided by University of Liverpool

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