

# **Dietary Fibre and the Prevention of Rheumatoid Arthritis**

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Dr Mario M. Zaiss



# DIETARY FIBRE AND THE PREVENTION OF RHEUMATOID ARTHRITIS

Rheumatoid arthritis is an autoimmune disease that results in painful and swollen joints, among other complications. Although treatment can alleviate the symptoms, more research is needed to understand the underlying causal mechanisms that could be exploited to prevent it. **Dr Mario Zaiss** the University of Erlangen-Nürnberg has carried out extensive research in this field and focuses on the impact of diet. He has made the exciting and important discovery that a high-fibre diet produces metabolites that play a vital role in preventing the onset of rheumatoid arthritis.

## An Autoimmune Disorder

Arthritis is a painful medical condition caused by inflammation in the joints. It comes in a number of forms, including osteoarthritis and rheumatoid arthritis. The latter type is an autoimmune disease which means that the immune system mistakenly attacks the cells lining the joint's cartilage, called the synovium. This also causes the release of disruptive chemicals that damage surrounding bones, ligaments, tendons and cartilage. As a result, the joint becomes stiff, swollen and painful and often, the sufferer experiences flare-ups in which the symptoms worsen for a period of time.

In addition to these symptoms, rheumatoid arthritis sufferers may experience fatigue, poor appetite and weight loss. They can also develop secondary complications due to the disease and these include carpal tunnel syndrome, a higher risk of heart attack and stroke, and inflammation in other areas of the body.

While there is no definitive cure for rheumatoid arthritis, thankfully we have treatments that can ease symptoms and minimise flare-ups. In fact, if caught and treated early enough, many patients can go years without a flare-up and go about their lives as normal. Therapies for rheumatoid arthritis include medicines that are continually taken, physiotherapy and sometimes surgery when necessary. If left untreated, the damage caused by the disease results in the loss of shape and alignment of the joint and possibly further destruction.

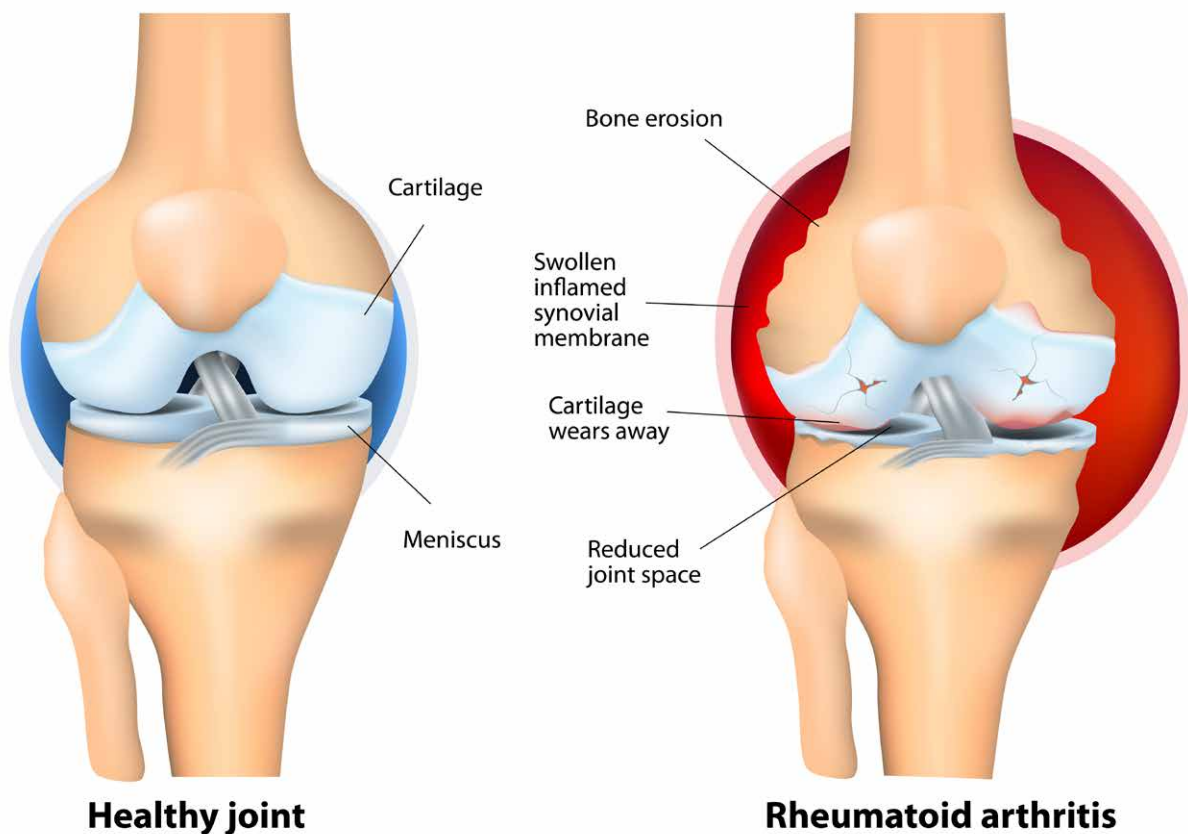
Precisely why the immune system suddenly begins to attack the joints is unclear. Currently, a number of risk factors are thought to contribute including genetics, smoking, older age and being overweight. As rheumatoid arthritis is more common in women than in men, this may be evidence for hormones like oestrogen contributing to its progression. New evidence is emerging that suggests the bacteria living in the gut, known as its microbiome, play an important role in the development and progression of rheumatoid arthritis.



Dr Mario Zaiss in the Institute for Clinical Immunology at the University of Erlangen-Nürnberg in Germany is studying this fascinating phenomenon. He has uncovered novel insights into how the microbiome plays into rheumatoid arthritis and how this information might be used in the future to help those suffering from it.

## Dietary supplements: Counteracting Inflammatory Effects

Dr Zaiss and his colleagues collated known information about the microbiome in relation to rheumatoid arthritis and built upon this. Patients with the disease had previously been observed to have microbial dysbiosis, a reduction in the diversity of beneficial



gut bacteria. Others who were at high risk of developing rheumatoid arthritis were also seen to have this disruption in the microbiome, supporting the idea that microbial dysbiosis is an environmental trigger for the illness.

Additionally, research has shown that diet impacts the natural balance (homeostasis) of the bacteria within the intestines. One important element of the diet is fibre, which can be soluble or insoluble. Insoluble fibre aids the movement of solids through the intestines, whereas soluble fibre is absorbed by certain gut bacteria and fermented to produce metabolites. Among the most abundant of these are short-chain fatty acids (SCFA) which serve as a source of fuel for intestinal epithelial cells and other bacteria types, consequently regulating the processes within the gut.

To pull these links together, Dr Zaiss provided rheumatoid arthritis patients with a high fibre diet in the form of cereals and cereal bars for a month. Blood and stool samples were taken and analysed before and after the month to compare different immune parameters. Following their fibre-supplemented diet, the patients displayed higher circulating regulatory T cells, which work to suppress the immune system to prevent autoimmunity and over-inflammation. Excitingly, they also showed decreased markers of bone erosion in their affected joints. Dr Zaiss believes these results could be utilised to supplement or complement existing pharmacological treatment approaches to rheumatoid arthritis.

A subsequent study by Dr Zaiss and his team continued to investigate the benefits of dietary fibre for rheumatoid arthritis. One of the regulatory roles of SCFA is as an anti-inflammatory, which was evidenced in the last study. It can promote regulatory T cells to carry out their function and some evidence suggests that they regulate other inflammatory immune molecules like chemokines. Therefore, Dr Zaiss wanted to investigate whether short-term, high-fibre interventions positively impacted rheumatoid arthritis patients by promoting the SCFA anti-inflammatory mediators.

They gave healthy controls participants high-fibre bars for 15 days and rheumatoid arthritis participants the same bars for 30 days. As hoped, their blood and stool samples revealed increased levels of SCFA and decreased cytokine concentrations. These two studies provide strong evidence that implementing a high-fibre diet alongside current drug therapies for rheumatoid arthritis could be highly practical and effective.

#### **Short-chain Fatty Acids: Preventing Disease Progression**

Dr Zaiss has followed this line of thinking in much of his research, including in very recent studies. Rheumatoid arthritis can develop slowly from the autoimmune phase where a person is at risk of more severe disease, to the clinical phase where pain and swelling become an issue. Therefore, Dr Zaiss investigated whether this progression can be prevented using his knowledge of dietary impacts and SCFA. Although SCFAs had been shown to inhibit the onset of clinical arthritis in models, this had not been studied in humans.





Dr Zaiss and his colleagues gathered 82 people who were deemed to be at high risk of developing rheumatoid arthritis, partly due to experiencing musculoskeletal pain but not joint swelling. Almost half of these participants developed clinical arthritis after an average of 6 months. After analysing everyone's blood samples, they discovered that the people who were at risk but never developed the clinical disease had significantly higher baseline levels of SCFA than those who did progress to more serious illness.

There are numerous types of SCFAs and the most noteworthy in this experiment were butyrate and acetate. Their data suggested they had the most influence over preventing the transition into clinical arthritis. Once again Dr Zaiss' research had shown that the dietary intervention of increasing fibre intake could greatly improve the prognosis of rheumatoid arthritis and even prevent it from forming into a much more problematic ailment.

### Identifying Underlying Mechanisms

Moving away from SCFAs, Dr Zaiss has also studied gut microbial dysbiosis and the mechanisms behind it that lead to rheumatoid arthritis. In autoimmune mice and humans, a peptide called zonulin is found in unusually high quantities. Zonulin has a vital part in regulating the tight junctions between cells that prevent water and its solutes from leaking where they shouldn't. When too much zonulin is present in gut cells, the intestinal barrier becomes leaky and dysbiosis and inflammation occur.

Dr Zaiss carried out mice model tests to investigate this issue to understand how it could be reversed. They found that high blood levels of zonulin can be used to predict the onset of clinical arthritis from asymptomatic autoimmunity but they



also defined certain molecules that could prevent disease. One of these was butyrate, which he found helped to restore the intestinal barrier before arthritis took hold. In addition, larazotide acetate, which works to prevent the action of zonulin, increased the integrity of the intestinal barrier to reduce the onset of arthritis. This study could be incredibly useful for developing drugs that minimise intestinal barrier damage in order to stop clinical rheumatoid arthritis from forming.

A final study from Dr Zaiss delves into a topic that many may find surprising. Research has shown that alcohol consumption can actually protect the body from autoimmune diseases like rheumatoid arthritis. However, the mechanisms behind this unusual occurrence were previously ill-defined. Again using mice models, Dr Zaiss demonstrated that alcohol metabolises into acetate in the body. The acetate alters the functionality of T helper cells which aids to regulate the immune system and prevent inflammation.

The effect of acetate on the T helper cells means that the production of autoantibodies (antibodies aimed against the host's body) is inhibited. Consequently, the autoimmune impacts of rheumatoid arthritis are reduced. Proving this link between T helper cells and autoimmunity, when Dr Zaiss tested immune responses without T cells, the progression of arthritis was not altered by alcohol consumption. This work provides an interesting look into the many complex biological pathways that are involved in rheumatoid arthritis and that have the potential to be exploited for future therapies.

Dr Zaiss' research provides fascinating insights into rheumatoid arthritis and has demonstrated that the diet of those at risk of rheumatoid arthritis or who already live with the disease could have a real impact on their medical outcomes.



# Meet the researcher

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Dr Mario Zaiss completed his basic studies in Marine Biology at the University of Bremen in Germany before moving to the University of Heidelberg where he received an MSc in Biology, majoring in Zoology and Ecology. He then went on to achieve his PhD in Immunology at the University of Erlangen-Nuremberg after which he carried out a number of research and postdoctoral roles. Dr Zaiss was a co-founder and project manager of a start-up company in Switzerland and currently serves as a Research Group Leader and a Professor for Immune Tolerance and Autoimmunity at the University of Erlangen-Nürnberg. His work concentrates on studying rheumatoid arthritis and how it may be prevented and treated.

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