

exercise and the gut microbiome

EXERCISE FOR THE PROMOTION OF A HEALTHY GUT MICROBIOME & HEALTHY GUT BARRIER THROUGH INCREASED *AKKERMANSIA MUCINIPHILA* - THE LINK TO POMEGRANATE & CURCUMIN

A healthy microbiome may have a tremendous impact on a person's overall wellbeing; the healthier it is, the healthier they are. The key to this – a delicate balance of nourishing the bacteria species that thrive in the gut. Tight junctions of the gut lining are carpeted with the microbiota that protect the GI tract against proliferation and colonization by unfriendly microbes and toxins.¹ When the gut becomes unhealthy, the tight junctions forming the lining can weaken, resulting in toxins and bacteria leaking into the bloodstream.^{2,3} This can then trigger a systemic inflammatory response throughout the body.^{2,3} Researchers explain that this increased gut permeability and resulting systemic inflammatory response has been linked to conditions like celiac disease and many other chronic illnesses.³ Overall, a healthier gut can be attributed to the fuel it is provided through nutrition and the balance of microbiota forming a symbiotic gut microbiome,⁴ as well as regular and consistent exercise.⁵

Exercise is known to raise an individual's core temperature and reduce blood flow to the intestines, which could lead to more direct contact between gut microbes and immune cells in the mucus layer of the gut, exhibiting a potential to shift microbial composition.⁵ Researchers explain, "exercise might alter gene expression of immune cells in the tissues of the gut, leading to the production of fewer pro-inflammatory cell-signaling proteins and more anti-inflammatory ones, as well as antioxidant enzymes."⁵ These immune cells sit near microbial communities in the gut and could produce antimicrobial compounds that tamp down certain taxa while bolstering the growth of beneficial probiotic bacteria, thus linking exercise and a healthy gut microbiome.⁵ "Exercise might also change the composition of the mucus in the gut, which would affect bacterial species that live there, such as *Akkermansia muciniphila*—a bacterium with anti-inflammatory properties that appears to increase in abundance in response to exercise."⁵

"*Akkermansia muciniphila* is a mucin-degrading bacterium that has been described to reside in the mucus layer and contributes to 3-5% of the microbial community in healthy subjects;" the gut is already colonized with *A. muciniphila*, which can be supported with prebiotics (the food for probiotics)⁶ and regular exercise.⁵

Cumulative research presents the link between a healthy gut microbiome and regular exercise.

Researchers have shown that exercise prevents weight gain and alters the gut microbes in a murine model examining diet-induced obesity.⁷

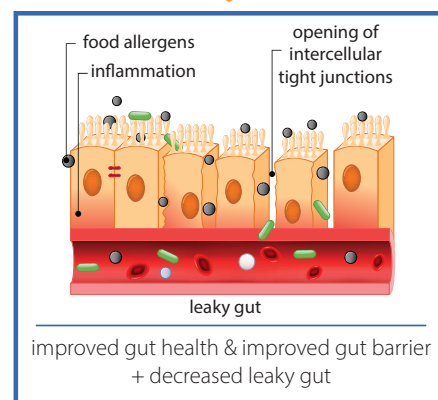
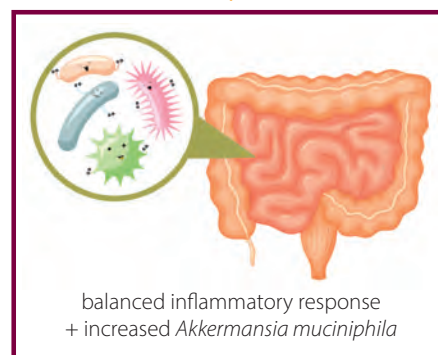
"[These results also align well] with a longitudinal study in humans... [t]hat found lean, sedentary people who exercised for six weeks also developed higher levels of *Clostridiales*, *Lachnospira*, *Roseburia*, and *Faecalibacterium* in their guts, but those microbes returned to baseline levels when the individuals stopped exercising.^[8] Obese individuals who started exercising had changes to their gut microbes too, but those changes were different than what was seen in lean individuals."^{5,[8]} *A. muciniphila* is naturally present in the healthy human digestive tract, and decreased abundance of *A. muciniphila* has also been correlated with increased body weight in humans,⁶ while increased abundance is common "in [people] with normal glucose tolerance compared [to] a prediabetic group."⁹ Further supporting this theory, research has shown "*Akkermansia*" has been associated with a lean BMI and improved metabolic health⁸ in people who exercised for little as three hours per week.⁸

"Overall, interesting evidence suggests that regular aerobic exercise confers benefits to the gut microbiota, which may be partially responsible for the widespread benefits of regular physical activity on human health."⁸

Consistency is key.

The effects of exercise in supporting a healthy gut microbiome "were both transient and reversible,"⁸ so consistency is required to maintain the potential benefits. Irregular and inconsistent exercise could result in an imbalance in the microbiome, or dysbiosis—"a microbial imbalance or maladaptation on or inside the body, such as an impaired microbiota"¹⁰—as well as increased permeability of toxins and disease. Dysbiosis can impact the immune system from the resulting antioxidant and reactive oxygen species (ROS) imbalance.¹ These highly reactive molecules are continually generated by cells

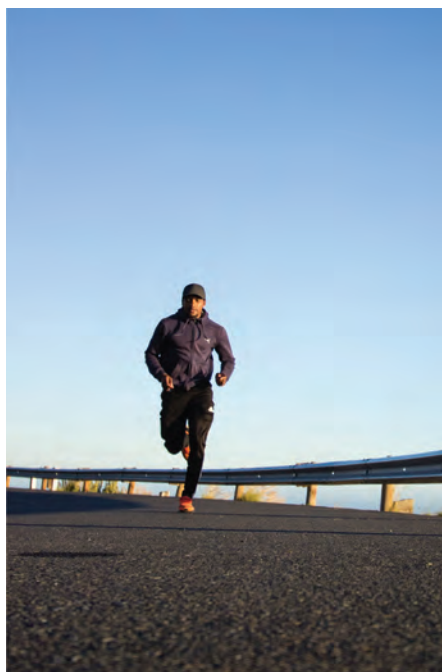
in the body as a natural byproduct through aerobic metabolism; this is the way the body produces energy. The generation of these reactive species induces oxidation of critical biomolecules, which may result in damage to cell structures. Cumulatively, this is known as oxidative stress. Antioxidants, paired with regular exercise, may offer a solution for the promotion of a healthy gut microbiome and healthy gut flora through their inflammatory impacts.



Restoridyn® is a patented polyphenol blend studied to advantageously hone in on the antioxidant properties of proprietary pomegranate and

curcumin extracts to offer a multi-prong solution. Clinical evidence suggests Restoridyn® is a synergistic solution offering an adaptogenic nutritional approach supporting recovery and immunity resulting in an increase in overall performance and stamina. Further, this antioxidant blend may also support a healthy gut microbiome.

In the gut, punicalagins from the pomegranate component of Restoridyn® are metabolized into urolithins; researchers detected these bioactive punicalagin derived metabolites within one hour after dosing.¹¹ This evidence, and additional research conducted by researchers at the University of Rhode Island, supports the breakdown of the punicalagins in Restoridyn® into urolithins by the microbiota in the gut.¹² Meanwhile, curcumin, the other half of Restoridyn®, “may sustain high concentrations in the intestinal mucosa, modulate gut barrier function, and thereby lower circulating bacterial [l]evels and inflammation to promote



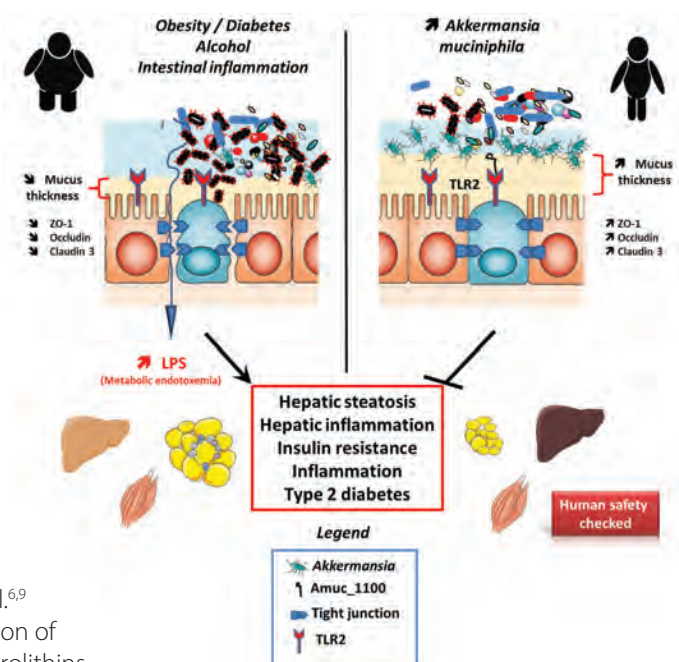
health effects. ...[c]urcumin supplementation restores intestinal barrier function and expression of tight junction proteins.¹⁴ Restoridyn may offer a multi-prong solution to promote a healthy balance of pro- and anti-inflammatory biomarkers that may foster a healthy gut and healthy gut microbiome, by means of the conversion of punicalagins to urolithins paired with mediation of the gut barrier through curcumin for a synergistic approach.¹⁵⁻¹⁷

In conjunction with knowledge that the punicalagins in Restoridyn® convert to urolithins in the gut,¹² researchers at the University of Rhode Island have conducted a preliminary study to examine the prebiotic effects of this pomegranate in a 12 week murine model featuring 16s rRNA sequencing of fecal content from low fat diet (LFD), high fat diet (HFD), and pomegranate supplemented diet (LFD and HFD) fed mice.¹³ Similar evidence suggests that conversion of punicalagins to urolithins in the human gut is vital to the successful promotion of Restoridyn's prebiotic potential.^{6,9} Researchers explain that conversion of pomegranate polyphenols into urolithins resulted in significantly higher *Akkermansia* in stool samples.⁶ The phenolic compounds in Restoridyn's punicalagins, for example, are metabolized by stomach acid, gastrointestinal enzymes, and by the gut microbiota.^{6,9,11} The hydrolysis of these antioxidant ellagitannins in the gut indicates that ingestion of Restoridyn's pomegranate component may stimulate the growth of *Akkermansia muciniphila*, thus acting as a prebiotic.¹¹

Akkermansia muciniphila has been shown to increase in abundance with regular exercise^{5,6,8,9} and polyphenols.¹⁸ Researchers explain that “polyphenols increase the secretion of mucin and remove reactive oxygen species (ROS), creating a beneficial environment for *Akkermansia muciniphila*.”¹⁸

A. muciniphila, and other beneficial bacterium, have also been shown to preserve the integrity of the intestinal mucus and intestinal barrier function, and counteract the detrimental effects of poor diet on gut permeability.¹⁸

Further, an abundance of *Akkermansia* is inversely correlated with bodyweight and with an improved metabolic profile.¹⁸



“The two-way interactions between polyphenols and the gut microbiota may contribute to host health benefits. This two-way interaction entails microbial degradation of polyphenols and modulation of gut microbiota by polyphenols and their metabolites, which inhibits pathogenic bacteria and stimulates beneficial bacteria.”¹⁸

Therefore, Restoridyn® may offer support for a healthy gut microbiome, as well as support recovery from exercise, improve immune health, and increase overall performance and stamina. Restoridyn® offers a multi-prong approach to not only impact gut flora and maintain a healthy gut, but also maintain a regular exercise regimen.

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Additional references may be found at vs-corp.com/ingredient-research/

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