# GASTROINTESTINAL HEALTH: gut & digestive support

## GO WITH YOUR GUT

The key to a healthy gut microbiome is a delicate balance of nourishing the bacterial species that thrive in the gut. Tight junctions of the gut lining are carpeted with the microbiota that protect the gastrointestinal (GI) tract against proliferation and colonization by unfriendly microbes and toxins.[1-2]

When the gut becomes unhealthy, the tight junctions forming the lining can weaken, resulting in toxins and bacteria leaking into the bloodstream.[2-4] This can then trigger a systemic inflammatory response throughout the body.[2-4] An imbalance in the microbiome can result in dysbiosis—"a microbial imbalance or maladaptation on or inside the body, such as an impaired microbiota."[5]

Overall, a healthier gut can be attributed to the fuel it is provided through active nutrition, the balance of microbiota forming a symbiotic gut microbiome,[6] and regular exercise.[2,7] The gut naturally hosts indigenous bacteria. Prebiotics may offer "enormous potential for modifying the gut microbiota, but these modifications occur at the level of individual strains."[8] Beyond simply supporting the gut with prebiotics, researchers explain that synbiotics, or the synergistic combination of both pre and probiotics, may be the most ideal solution in promoting a healthy gut microbiome.[8]

Pomella® supports a potential botanical solution for a multi-pronged approach to health.

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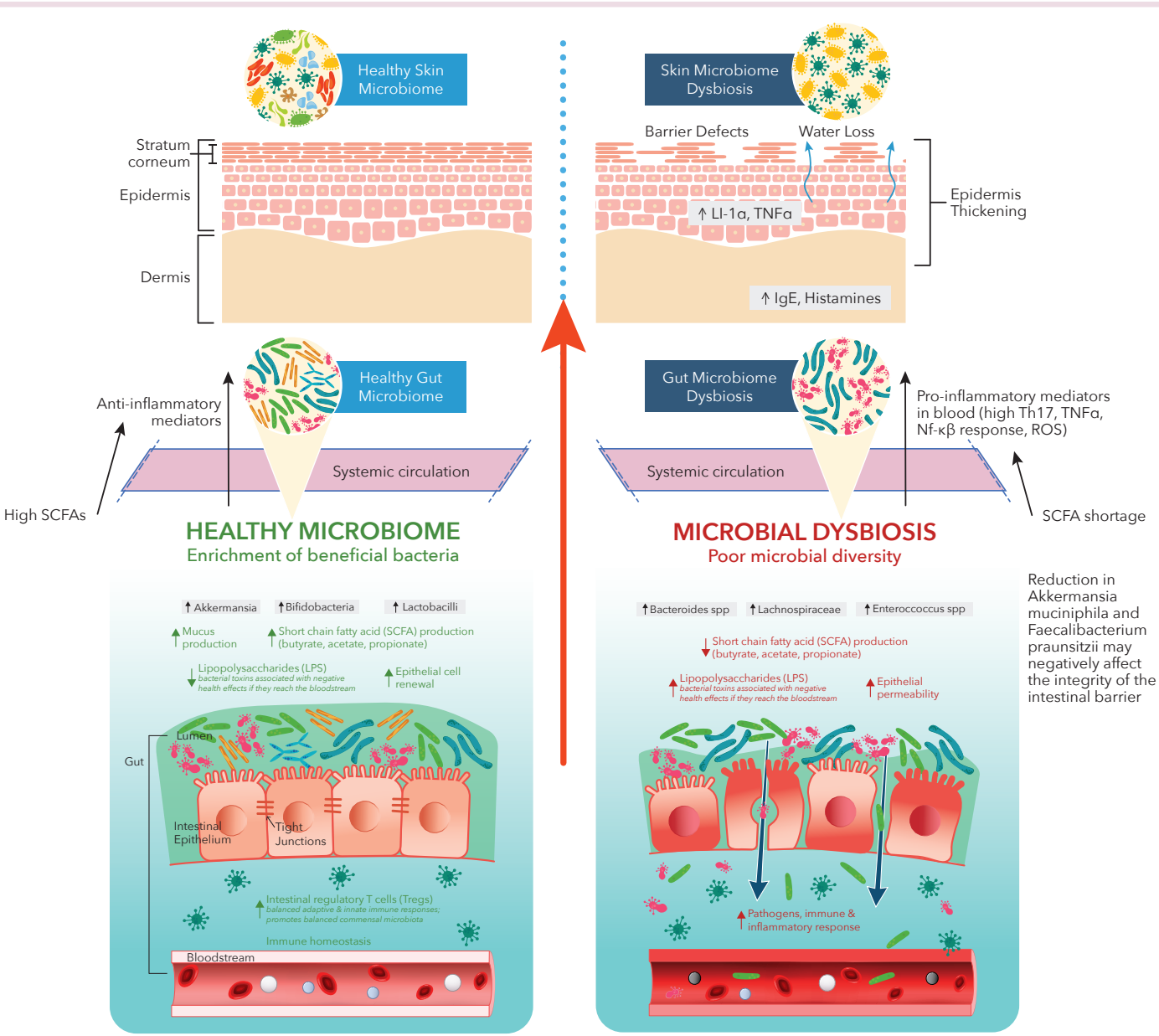
pomella® POMEGRANATE EXTRACT

# POLYPHENOLS AND THEIR ABSORPTION: THE ROLE OF THE GUT MICROBIOTA

General consensus has been reached on the importance of a healthy gut barrier for systemic health. Human and animal studies confirm that the intestinal microbiota contribute to the function, or dysfunction, of distant organs in the body, beyond the gut.[9] Short chain fatty acids (SCFAs), products of the metabolism of the gut microbiome (butyrate, acetate, propionate), show a protective role against the development of inflammatory disorders, strengthening the natural intestinal barrier and exerting a direct anti-inflammatory effect.[10]

The gut microbiome's influence clearly goes beyond the gastrointestinal system. One target organ known to have a particular connection with the gut, is the skin.[9] Gut dysbiosis negatively impacts on the skin barrier integrity and physiological functions.[11] The gut-skin axis includes several ways to develop this reciprocal communication.



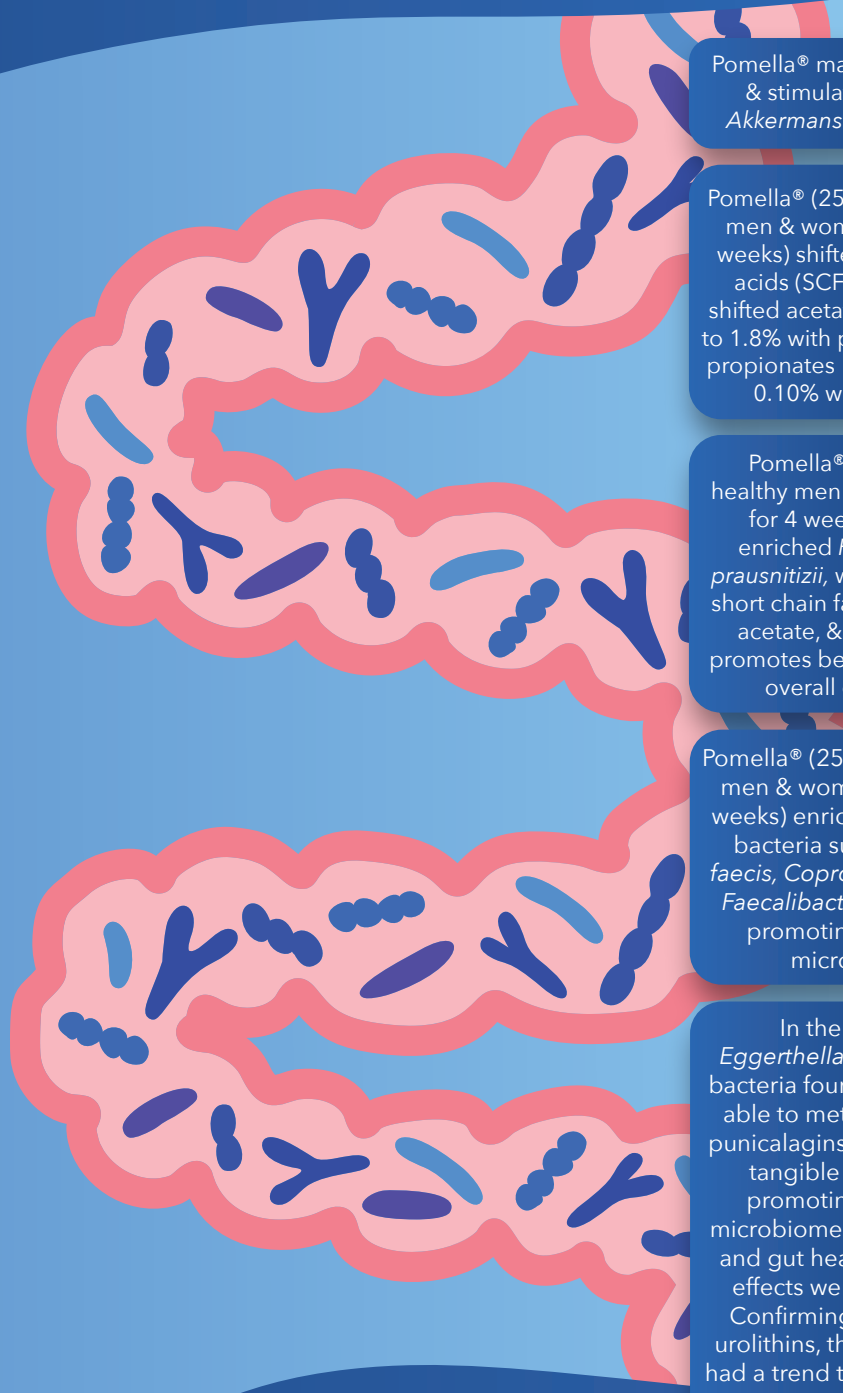

*The gut-skin axis explained: in the left panel a healthy gut-skin connection is represented; in the right panel the dysbiotic gut microbiota is shown, with increased intestinal permeability affecting the skin health, systemic inflammation and finally, skin disorders, happening as a consequence of the barrier integrity's loss. SCFAs (short-chain fatty acids); TNFα (tumor necrosis factor alpha); NF-kB (nuclear factor kappa-light-chain-enhancer of activated B cells); ROS (reactive oxygen species)*

# PREBIOTIC EFFECTS: INTESTINAL BARRIER INTEGRITY

*Akkermansia* is "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,[12] in fact, *Akkermansia* is found in more than 95% of the population.[13]

*Akkermansia muciniphila*, and other beneficial bacterium, have 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.[14] Researchers at the University of Rhode Island have conducted a preliminary study to examine the prebiotic effects of Pomella® in a12-week murine model featuring 16s rRNA sequencing of fecal content from low fat diet (LFD), high fat diet (HFD), and Pomella® supplemented diet (LFD and HFD) fed mice.[15] Pomella® may act as a prebiotic and stimulate the growth of *Akkermansia muciniphila*.[12-19]

Evidence of the antioxidant, anti-inflammatory and anti-glycative effects of Pomella® are well supported by in vivo and in vitro studies. Studies on its bioactive absorption also support the bioavailability of the functional molecules, upon digestion and metabolism mediated by the intestinal microbiota. Pomella® exerted an ability to modulate the gut microbiota composition, with an increase in the presence of *Akkermansia*, and thus a thicker mucus layer and a better defense of the intestinal barrier.



Pomella® may act as a prebiotic & stimulate the growth of *Akkermansia muciniphila*.[12-19]

Pomella® (250mg/day in healthy men & women 22-55yrs for 4 weeks) shifted short chain fatty acids (SCFAs).[14-16] Pomella® shifted acetates 38% (compared to 1.8% with placebo) and shifted propionates 162% (compared to 0.10% with placebo.[21-23]

Pomella® (250mg/day in healthy men & women 22-55yrs for 4 weeks) significantly enriched *Faecalibacterium prausnitizii,* which produces key short chain fatty acids; butyrate, acetate, & propionate, and promotes better gut barrier and overall gut health.[21-23]

Pomella® (250mg/day in healthy men & women 22-55yrs for 4 weeks) enriched beneficial gut bacteria such as *Roseburia faecis, Coprococcus eutacus,* & *Faecalibacterium prausnitizii*, promoting a healthy gut microbiome.[21-23]

In the presence of *Eggerthellaceae*, a species of bacteria found in the gut that is able to metabolize Pomella's punicalagins into urolithins, the tangible health benefits promoting a healthy gut microbiome, better gut barrier, and gut health, the beneficial effects were compounded. Confirming conversion into urolithins, the Pomella® group had a trend to increase urolithin concentrations by 6.6%.[21-23]

# SHORT CHAIN FATTY ACIDS

Similar to the benefits seen with *Akkermansia*, "a longitudinal study in [healthy] 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."[14,20]

In a randomized, double-blind, placebo-controlled trial in healthy adults aged 25-55yrs (n=18, men & women), a single capsule of 250mg Pomella® (from *Punica granatum*) was administered orally each day for 4 weeks. Researchers examined shifts in gut microbiome diversity and shifts in blood short chain fatty acid (SCFA) levels. Short chain fatty acids can act as postbiotics, or the bioactive byproduct of probiotics and prebiotics, in signaling from the gut to other areas of the body. In particular, butyrate, propionate, and acetate are key short chain fatty acids known to support the gut-body axes.[21-23]

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In the gut, *Roseburia faecis* and *Coprococcus eutacus* were significantly enriched at 4 weeks with Pomella® (250mg) compared to the control. These are beneficial gut bacterial species and promote a **healthy gut microbiome**.[21-23]

*Faecalibacterium prausnitizii* is found in abundance in a healthy gut microbiome and is known to produce short chain fatty acids (SCFAs). Because of this ability to produce SCFAs; enrichments of these beneficial bacteria also pertain to **better gut barrier** and **better gut health**. Pomella® (250mg) significantly enriched *Faecalibacterium prausnitzii* at 4 weeks compared to the control.[21-23]

Impacts to propionate and acetate are of particular importance as it sheds light into systemic circulation and gut-body axes.[14] Researchers found **short-chain fatty acids (SCFAs) shifted** in the Pomella® group with a 38% (vs 1.8% in placebo) in acetates and 162% (vs 0.10% in placebo) in propionates.[21-23]

*Eggerthellaceae*, a species of bacteria found in the gut that is able to metabolize Pomella's punicalagins into urolithins, can compound the beneficial effects. The Pomella® group had a trend to increase **urolithin** concentrations by 6.6%.[14-16] This supports previous data and shows that not only does Pomella® shift the gut microbiome, but also reacts to the specific bacterial strains as well.[16,17,21-23*]

# COMPOUNDING BENEFITS

"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."[14]

*Eggerthellaceae*, a species of bacteria found in the gut that is able to metabolize Pomella's punicalagins into urolithins, can compound the beneficial effects. Researchers observed statistically significant shifts for individuals with an overexpression of *Eggerthellaceae* in their gut, meaning that while all subjects taking Pomella® showed significant improvements, this subset showed even greater improvements. Further, the Pomella® group had a trend to increase urolithin A concentrations by 6.6%.[21-23] This supports previous data and shows that not only does Pomella® shift the gut microbiome, but also reacts to the specific bacterial strains as well.[16,17,21-23*]



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