BEAUTY FROM WITHIN: POMELLA'S EFFECTS ON DIGESTIVE & SKIN HEALTH

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HOMEOSTASIS A SKIN-GUT AXIS APPROACH

The symbiotic relationship between phenolic compounds and gut microbiota have gained attention due to their relevance in supporting human health, specifically in their role for gut/digestive support as well as skin health and beauty from within. In particular, pomegranate has long been associated with possessing high content of antioxidant polyphenols, in particular ellagitannins such as punicalagins and their gut-derived metabolites, urolithins.

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]

The increased gut permeability results in microbiome dysbiosis. This imbalance also influences the skin microbiome.[4] "Cumulative evidence has demonstrated an intimate, bidirectional connection between the gut and skin, and numerous studies link gastrointestinal (GI) health to skin homeostasis and allostasis [the body's adaptogenic response to return to homeostasis]."[4] There is evidence that "the intestinal microbiome may impact cutaneous physiology, pathology, and immune response more directly, through the metastasis of gut microbiota and their metabolites to the skin. In cases of disturbed intestinal barriers, intestinal bacteria as well as intestinal microbiota metabolites have been reported to gain access to the bloodstream, accumulate in the skin, and disrupt skin homeostasis."[4]

- **32%** — 32% increase in antioxidant activity in blood plasma 0.50hr after the consumption of a single dose of Pomella[14]
- Urolithins detected in the body up to 7 days after dietary ellagitannin intake[20,21]
- Supports skin health against UVA- and UVB-induced damage[11]
- Pomella® ranked highest in antioxidant activity across a number of assays including ORAC, TEAC, FRAP, and DPPH, compared to 26 other antioxidant products[23]

SUGGESTED DAILY DOSE

for gut health as a prebiotic:

180-240mg/day

for skin health through antioxidant support:

200-300mg/day

Published clinical studies suggest that a plant-derived diet rich in antioxidants may exert prebiotic effects, namely, a positive impact on the growth or activity of beneficial microorganisms, to ameliorate health conditions.[5] Although pomegranate ellagitannins, including punicalagin, are not absorbed intact into circulation, they undergo hydrolysis in the acidic environment of the stomach and are digested by intestinal enzymes to yield ellagic acid, the hydrolysis product of ellagitannins. The unabsorbed ellagitannins and ellagic acid are further converted by gut microbiota in the large intestine to produce a group of gut microbial metabolites known as urolithins.[6]

Several studies have demonstrated that Pomella® and its bioactive compounds including punicalagin and ellagic acid, as well as their gut microbial metabolites, urolithins, exert promising health benefits. For instance, Pomella can reduce the formation of advanced glycation endproducts (AGEs), which are a series of macromolecules that contribute to many digestive issues including irritable bowel syndrome and ulcerative colitis,[7,8] and lead to oxidative stress,[9] which can contribute to collagen cross-linking (which causes wrinkles), inflammation, inhibited skin cell growth, and accelerated aging.[10-13]

WHY POMELLA?

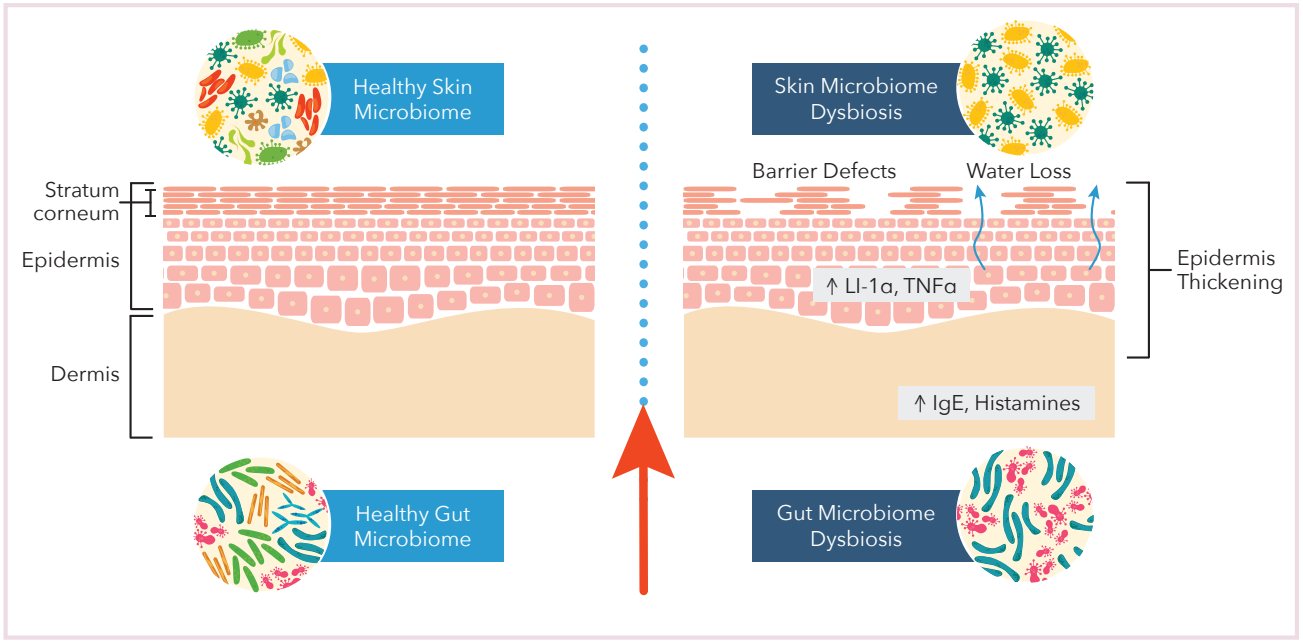
- Exhibits protective effects from UVA/UVB induced damage
- AGE interrupter supporting healthy skin aging against glycative effects
- Antimicrobial properties
- Contains 50% polyphenols
- Patented & proprietary *Punica granatum* extract
- Standardized to punicalagins
- Non-GMO Project Verified
- Self-GRAS affirmed

PREBIOTIC POTENTIAL - GUT & DIGESTIVE SUPPORT

In the gut, punicalagins from Pomella are metabolized into urolithins; researchers detected these bioactive punicalagin derived metabolites within one-hour after dosing.[14] This evidence, and additional research conducted by researchers at the University of Rhode Island, supports the breakdown of Pomella's punicalagins into urolithins by the microbiota in the gut.[15]

The gut naturally hosts indigenous bacteria, and prebiotics may offer "enormous potential for modifying the gut microbiota, but these modifications occur at the level of individual strains."[16] 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.[16]

"*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.[17] They are naturally present in the healthy human digestive tract, though decreased abundance of *A muciniphila* has also been correlated with increased body weight in humans,[17] while increased abundance is common "in [people] with normal glucose tolerance compared [to] a prediabetic group."[18]



Researchers summarized that "*A muciniphila* may play an important role in the healthy gut microbiome."[17] Given the natural presence in the human colon and overall impact on healthy gut microbiome, *A muciniphila* is an ideal bacterial strain (probiotic) to examine synergistic potential with prebiotic supplementation. In conjunction with knowledge that Pomella's punicalagins convert to urolithins in the gut,[15] researchers at the University of Rhode Island have conducted a preliminary study to examine the prebiotic effects of Pomella® in a 12-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.[19] Similarly, evidence suggests that conversion of punicalagins to urolithins in the human gut is vital to the successful promotion of pomegranate extract's prebiotic potential[17,18] Researchers explain that conversion of pomegranate polyphenols into urolithins resulted in significantly higher Akkermansia in stool samples.[18] The phenolic compounds in Pomella's punicalagins, for example, are metabolized by stomach acid, gastrointestinal enzymes, and by the gut microbiota.[14,17,18] **The hydrolysis of these antioxidant ellagitannins in the gut indicates that ingestion of Pomella may stimulate the growth of *Akkermansia muciniphila*, thus acting as a prebiotic.**[14]

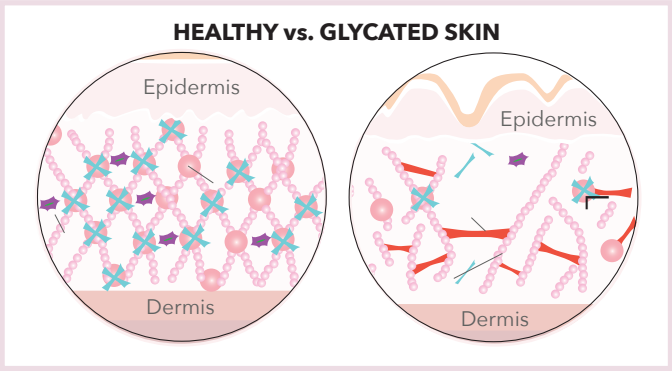
SKIN HEALTH FROM WITHIN

The polyphenolic compounds that support the gut/digestive health by modulating gut microbiota also support skin health from within. In vitro studies using aerobically cultured bacteria showed that treatment with pomegranate phytochemicals including its major ellagitannin, punicalagin, lead to the growth inhibition of pathogenic strains including clostridia and *Staphyloccocus aureus*.[20,21] In addition, pomegranate ellagitannins contributed to the up-regulation of the growth of probiotic Bifidobacteria including *Bifidobacterium breve* and *Bifidobacterium infantis*.[20,21] **This suggests Pomella's potential for a synbiotic approach to gut and skin health.**

It has been shown that in cases of gut / microbiota dysbiosis, the skin is also in a state of disrepair; "in cases of disturbed intestinal barriers, intestinal bacteria as well as intestinal microbiota metabolites have been reported to gain access to the bloodstream, accumulate in the skin, and disrupt skin homeostasis."[4] Therefore, Pomella® may offer synergistic potential as an oral application to answer consumer demand for beauty from within products - not only in support of gut and digestive health, but also in areas of support for skin health through its antioxidant potential.

pomella® NATURAL POMEGRANATE EXTRACT

Pomella may offer skin health benefits through the promotion of a healthy gut as "the gut microbiome has also been shown to support restoration of skin homeostasis after ultraviolet (UV) radiation exposure."[4] When skin is exposed to oxidative stress, the effectiveness of the endogenic antioxidant system (produced by the body rather than consumed) can be significantly compromised. Ultraviolet light exposure causes an increase in the production of reactive oxygen species (ROS) within cells, leading to oxidative stress and photodamage to proteins and other macromolecules on the skin. It is also responsible for inflammation, immunosuppression, oxidative DNA damage, and increased expression of metalloproteinases (MMPs) that are apart of collagen degradation. This inflammatory response is due to the activation of transcription factor nuclear factor-kB (NF- kB), which leads to collagen fiber breakdown, and results in the typical pattern of wrinkled, rough, dry and brown pigmented skin.



In vitro data supports Pomella's beneficial effects against UVA- and UVB-induced damage attributed to reduced generation of intracellular ROS and increased intracellular antioxidant capacity.[11]

As one ages and skin is exposed to UV light, collagen fibrils structurally modify because of glycation. One of the consequences of AGEs are cross-links, which degrade skin's extracellular matrix by chaining the proteins together. Cross-linking reduces elasticity in softer tissues such as the skin. Pomella® not only exerts anti-glycation properties but also has the ability to inhibit cross-linking.[9,10-13] Pomella mediates glycation, collagen cross-linking induced by glycation, and reducing the degradation of skin-protecting proteinsby inhibiting the enzymes (collagenase and elastase) that breakdown collagen and skin elasticity. Thus, Pomella promotes healthy skin aging through, reduced oxidative stress, cellular function and rejuvenation.

In addition to skin integrity and structure, Pomella may promote a balanced dermal microbiome and modulate facial sebum (oil) production. In topical studies Pomella's punicalagins showed 10 to 60% reduction in sebum production, and in an oral study there was also a reduction of facial sebum production.[22 *]

POMELLA'S DEFENSE AGAINST GLYCATIVE STRESS

Collagen is the glue that holds the skin together and creates a functional skeletal structure. Without collagen, skin is less elastic, thinner, and has greater appearance of wrinkles. Pomella® helps collagen defend against glycative stress.

SUMMARY

Overall, findings from pre-clinical and human clinical studies support pomegranate ellagitannins, namely punicalagins and their gut microbial metabolites, urolithins, can: 1) exert prebiotic effects to enhance the growth of beneficial bacteria; 2) alleviate gut microbial imbalance induced conditions; 3) promote gut/digestive health by mediating the balance of pro- and anti-inflammatory status; 4) offer skin health support through a balanced skin-gut microbiome; 5) promote supple skin through collagen and elastin maintenance & AGE inhibition, 6) support dermal and skin appearance from within.

Taken together, Pomella's polyphenols and gut microbial metabolites contribute immensely to the health benefits associated with skin-gut axis. Consequently, Pomella, a patented pomegranate fruit extract standardized to deliver bioactive phytochemicals including punicalagins, is a promising solution supporting gut and digestive health, skin health, and beauty from within.

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* For more references, visit: marketing.vs-corp.com/pomella-science