

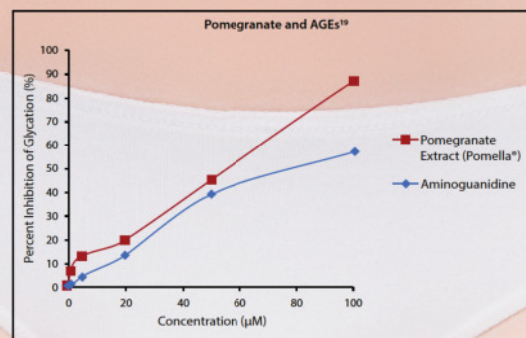
SKIN-GUT AXIS: the potential of POMEGRANATE

By Nikeeta Kheradia and Sonya Cropper

Daily exposure to ultraviolet light (UV) radiation can lead to a range of skin conditions that vary from early aging to more deadly concerns, such as immunosuppression and skin cancer. Preventive measures for skin damage typically include avoiding and blocking the sun, which is not always possible. Thus, there is a need for naturally derived solutions to protect the skin from damage.

Over the years, researchers have studied various botanical ingredients that act as natural sources of antioxidants to repair and rebuild skin. Examples of active ingredients and their sources have included, berries and red cabbage for cyanidins; grapes for resveratrol, apples and evening primrose for quercetin, and milk thistle for silymarin.¹ Many of these concepts are derived from historic use, such as Ayurvedic medicine. More recently, researchers have studied plant-based polyphenols with historic use in India, particularly the pomegranate (*Punica granatum* L.).

"Pomegranate extract is a top candidate among other polyphenolic botanicals for skin health," says Hang Ma, PhD, lead researcher and Research Associate in the



Department of Biomedical and Pharmaceutical Sciences in the College of Pharmacy at the University of Rhode Island.

Dr. Ma has studied pomegranate extensively and finds that not all forms and extracts present the most benefits for bioavailability. He says Pomella® Extract, from Verdure Sciences, is the gold standard among all other pomegranate extracts. Pomella contains the ideal

constituents of ellagitannins and punicalagins (PA) to form the bioactive metabolites for antioxidant related health benefits. As you will see, pomegranate extract possesses unique protective effects against UVA- and UVB-induced damage to the skin.

POMEGRANATE AND PUNICALAGINS

Dr. Ma warns that too often companies use ellagic acid (EA) levels as a measure of potency and efficacy for

products like pomegranate juices and extracts. In truth, he says, they should measure punicalagin.

Punicalagins, a group of potent antioxidants unique to the pomegranate fruit, are water soluble, highly bioavailable, and supported by safety data. They are also shown to possess a high absorption rate. Not only are punicalagins known to offer a powerful kick of antioxidant properties on their own, they are

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among the most ferocious scavengers of free radicals, or unstable molecules that can cause damage to skin over time.

They also display other interesting activities, such as potent modulation of inflammation and protective effects of DNA and cellular signaling. Punicalagins are unique because they are able to break apart, or hydrolyze, into smaller polyphenols (such as ellagic acid) once in the bloodstream, where they metabolize and absorb into target tissues.

Despite that, many still use EA levels as a biomarker for efficacy; however, they don't translate to bioavailability or efficacy because ellagitannins are poorly absorbed in the intestines and therefore never reach physiologically significant concentrations in the bloodstream. “However, once ellagitannins and ellagic acid enter the gut and interact with the microbiome, their metabolites form into urolithins,” Ma says. This skin-gut axis interaction is what makes pomegranate a remarkable ingredient for skin care.

SKIN-GUT AXIS AND POMEGRANATE EXTRACT

Pomegranate extract (PE) is unique in that it acts like a prebiotic in the gut.² Emerging research shows that prebiotics can be a protective agent against the onset of atopic dermatitis in children and UV pigmentation in adult skin.^{3,4} This novel combination of antioxidant and gut metabolite puts PE in a unique category as a skin protector that is tied to the skin-gut axis.⁵

“The skin and the gut have more similarities than one would suppose ... Both contain rich vascular supply, diverse microbial communities, and act as vital interfaces between the internal human body and the external environment,”

-World Journal of Dermatology.⁶

Scientists are only just learning how the cellular and structural makeup of the skin impacts the skin's immune response. However, research shows that metabolites from one's diet or microbiota are accessible to the skin.⁷ A closer examination of gut-skin dysbiosis disorders, such as the link between Crohn's and psoriasis, or stress-induced skin conditions, gives us clues as to the interface between organs; the gut and the skin.⁸ There is evidence that surface microbes interact with the deeper microbial components, as well as deeper immune cells and pathways through a complex dialogue that makes up the skin-gut axis.⁹

Though the exact mechanisms are still being determined, it is believed that “intestinal microflora produce neurotransmitters in response to stress and other external stimuli that could modulate skin function via neural pathways.”⁵

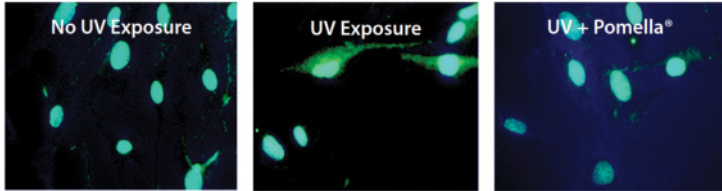
Now that it is understood that the skin and organs are closely linked through the skin-gut axis, the role of prebiotics for skin health is also becoming a strong opportunity. Pomegranate extract has been shown to increase the mean counts of beneficial bacteria *Bifidobacterium* and *Lactobacillus* and significantly inhibit the growth of harmful bacteria *B. fragilis* group, *clostridia*, and *Enterobacteriaceae* in a dose response manner.¹⁰ In a study in Beneficial Microbes (2014), researchers concluded, “In cosmetic formulations, prebiotics can be applied to the skin microbiota directly and increase selectively the activity and growth of beneficial 'normal' skin microbiota.” ... “Nutritional products containing prebiotics (and/or probiotics) have a positive effect on skin by modulating the immune system and by providing therapeutic benefits for atopic diseases.”¹¹



SKIN DEGRADATION FROM UV EXPOSURE

The skin has a very effective way of protecting itself through the

EFFECT ON SKIN FIBROBLASTS



endogenous antioxidant system. This system contains a variety of enzymes, such as glutathione peroxidase, glutathione reductase, catalase and superoxide dismutase, which degrade hydrogen peroxide, lipid hydroperoxides and superoxide.¹² When skin is exposed to oxidative stress, the effectiveness of the endogenous antioxidant system 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.

POMEGRANATE AND THE FORMATION OF ADVANCED GLYCATION END-PRODUCTS

The internal workings of the skin start with collagen. As we age, we all need more collagen because the skin's structural proteins are vital to skin's

mechanical framework and cellular processes. However, collagen protein has a very slow turnover rate and is particularly susceptible to modification by glycation and

oxidative stress (see the glycated skin image). Skin collagen has a half-life of about 15 years.

The internal workings of the skin start with collagen. As we age, we all need more collagen because the skin's structural proteins are vital to skin's mechanical framework and cellular processes. However, collagen protein has a very slow turnover rate and is particularly susceptible to modification by glycation and oxidative stress (see the *glycated skin image*). Skin collagen has a half-life of about 15 years. Over one's lifetime, it undergoes up to a 50% increase in glycation because of sun exposure.¹³

WHY POMELLA?

- Exhibits protective effects from UVA/UVB induced damage
- AGE interrupter
- Actively supports healthy aging against glycative effects
- Antimicrobial properties
- Contains 50% polyphenols
- Patented & proprietary *Punica granatum* extract
- Standardized to punicalagins
- Natural, whole pomegranate spectrum
- Non-GMO Project Verified
- Self-GRAS
- Additional grades available: food grade, organic, and more

Over one's lifetime, it undergoes up to a 50% increase in glycation because of sun exposure.¹³

Glycation impairs collagen in the following ways:

- The formation of advanced glycation end products (AGEs) alters collagen's protein charge, interferes with its active sites, and alters collagens ability to act properly with surrounding cells and matrix proteins,¹⁴
- Intermolecular cross-linking modifies collagen's biomechanical properties,¹⁵

Pomegranate, a natural advanced glycation end products (AGEs) inhibitor and anti-inflammatory agent, shows great potential for anti-glycation, a major contributor to slowing the progression of skin damage. Recent research shows that the phenolics in pomegranate play a unique role in the inhibition of the production of ROS and the formation of AGEs from protein glycation.¹⁶

Researchers investigated the potential protective effects of a

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.

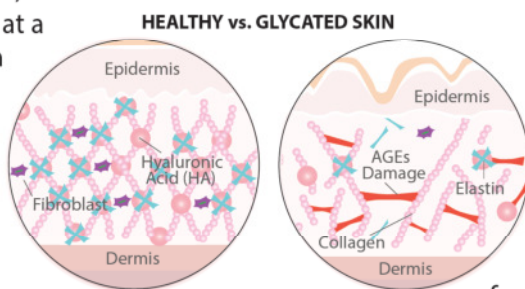
pomegranate extract (PE) with standardized punicalagins against UVA- and UVB-induced damage in human skin fibroblast cells. The PE, in a range of 5 to 60mg/L, was effective at protecting human skin fibroblasts (SKU-1064) from cell death following UV exposure. This is attributed to reduced generation of intracellular ROS and increased intracellular antioxidant capacity.

POMEGRANATE PHENOLICS INHIBIT TYPE 1 CROSS-LINKING

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. Phenolic-rich plant foods, such as PE, exert not only anti-glycation properties but also have the ability to inhibit cross linking.

For instance, a pre-published study shows that the pomegranate phenolics, punicalagin (PA), ellagic acid (EA) and urolithin (UA) at a concentration of 200 uM,

inhibit fructose induced collagen glycation by 64.4%, 15.0%, and 17.3%, respectively.¹⁷ The same concentration inhibited methylglyoxal (MGO) induced collagen by 70.6%, 17.6%, and 14.4%, respectively. Findings also showed an inhibition in the formation of Amadori products (non-enzymatic carbohydrate modification) when skin cells were exposed to PA, EA, and



Pomegranate and Skin Care from Within: Pomegranate Extract's Skin Protecting Benefits

- Inhibition of Advanced Glycation Endproducts (AGEs)
- Supports Collagen Protection from Glycative Stress
- Methylglyoxal (MGO) Scavenging Effects
- Protective effects against Oxidative Stress
- Supports Elastase Inhibition

UA, at 200 uM concentration, 45.7%, 31.5%, and 40.0%. These results show that PA may provide a novel therapy to reversing collagen glycation and cross-linking as it relates to skin damage.

In summary, there is evidence that standardized pomegranate extracts are a valuable solution to the degenerative effects of UV exposure, including glycative stress and cross-linking. As we

learn more about the role of prebiotics for skin health, PE is rising to the top as a viable option for a skin and beauty from within ingredient.

Pomegranate extract's unique status as a prebiotic, places it in a valuable position as a skin-gut axis ingredient.

As more is learned about the role of prebiotics on the skin's microbiome, PE stands out as a consumer-friendly ingredient for skin health. And, since botanical extracts are complex

compounds with multiple phytochemicals, there are notable benefits to choosing a full spectrum plant extract, such as Pomella pomegranate extract, rather than an isolated compound. For companies seeking a strategy to address the contributing factors to skin conditions, this research presents strong potential for pomegranate's skin healing properties.

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FOR MORE INFORMATION:

POMELLA® is a part of the Gee Lawson range of ingredients distributed in Europe by LeHVoss.



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