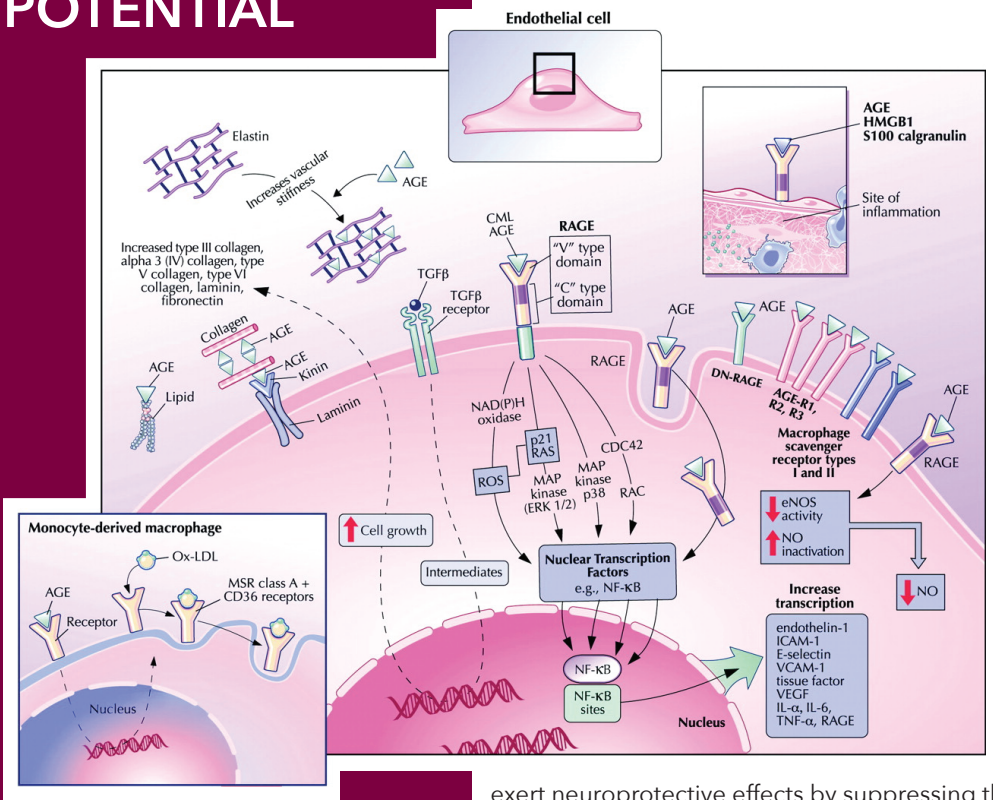


# POMELLA'S ANTIOXIDANT POWER IMPACTS SYSTEMIC INNATE IMMUNE POTENTIAL

Pomella®, a patented natural pomegranate fruit extract standardized to deliver measurable and efficacious bioactive phytochemicals including punicalagins and metabolites, is a powerful antioxidant with a variety of health beneficial effects. A large body of published laboratory-based, preclinical, and clinical studies support Pomella's antioxidant ability to effectively inhibit the formation of advanced glycation endproducts (AGEs), a group of detrimental chemicals derived from sugar metabolism.<sup>1</sup> Notably, the inhibitory effects of Pomella® against oxidative stress compounds, or AGEs, is backed by a human clinical study showing that Pomella® (150mg twice daily for one month) reduces the levels of glycated hemoglobin (HbA1c), a clinical biomarker of AGEs.<sup>2</sup> Further, a double-blind, placebo-controlled trial showed that Pomella®, as an adjuvant to medication for myocardial infarction, decreased cardiac risk factors, improved plasma antioxidant status, and reduced biomarkers including serum homocysteine, hs-CRP and OX-LDL.<sup>3</sup>



AGEs are known to play a pivotal role in glucose homeostasis and immune health and together with their precursors, for example, reactive carbonyl species, such as methylglyoxal, are formed during the oxidation of glucose and biomacromolecules including protein and lipids. Abnormal amounts of accumulated AGEs can aggravate several conditions including chronic inflammation, oxidative stress, endothelial dysfunction, insulin resistance, and other immune disorders.<sup>4</sup>

Pomella's beneficial immune effects may be exerted via the modulation of the receptor for AGE, known as RAGE; an immunoglobulin type of transmembrane receptor expressed at low levels in normal tissues and in the vasculature. RAGE becomes upregulated in tissues where AGE levels accumulate, consequently exacerbating inflammatory and stress-related cardiometabolic disorders<sup>5</sup> and certain neurodegenerative diseases.<sup>6</sup>

It has been reported that phenolics in pomegranate can reduce the level of several RAGE ligands including AGEs<sup>1</sup> and amyloid beta protein.<sup>7</sup> Therefore, Pomella's AGE scavenging capacity may impede RAGE from binding to its ligands, which may lead to down-regulating of RAGE expression. Moreover, phenolics in Pomella® may also mediate innate immunity related molecular targets, such as the NLRP3 inflammasome and toll-like receptors (TLRs), that are involved in RAGE associated inflammatory conditions.<sup>8</sup>

Notably, RAGE is highly expressed on the membrane of microglial cells, specialized macrophages which serve as resident brain immune health cells in the central nervous system (CNS) and play an innate role in mediating inflammatory cytokines thereby modulating brain health. RAGE is a transporter for the influx of beta amyloid peptides (Aβ), a pathological hallmark of cognitive decline, from the periphery to the CNS. Subsequently, elevated levels of RAGE ligands including AGEs and Aβ lead to several immune responses including the secretion of pro-inflammatory cytokines and increased oxidative stress. Published studies support pomegranate phytochemicals exert neuroprotective effects by suppressing the abnormal hyperactivation of microglial cells to reduce oxidative and inflammatory stresses.

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These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.

Please note that the physiological activity of the ingredient(s) described herein is supported by the referenced clinical trial report(s). Marketers of finished products containing the ingredient(s) described herein are responsible for determining whether claims made for such products are lawful and in compliance with the laws of the country in which they will market the products.

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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.<sup>11</sup> 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.<sup>12</sup> 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.<sup>13-15</sup>

Evidence suggests Pomella®, its punicalagins and metabolites may be associated with health promoting benefits for cellular, cardiometabolic, microglial, gut, skin, and immune functions frequently disrupted with oxidative stressors from aging, environmental, or diet.<sup>9</sup>



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