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Pomanox® and longevity science: Connecting mechanisms of healthspan from cells to humans

Living longer is no longer the challenge of our time. The real goal today is to extend the years of life spent in good health, the *healthspan*.

Healthy longevity depends on maintaining balance in the body's key systems: immune, metabolic, vascular, and cognitive. Over time, however, a subtle form of inflammation known as inflammaging disrupts that balance.

Inflammaging, a persistent, low-level immune activation, results from oxidative stress, the buildup of reactive oxygen species (ROS) that accelerate tissue decline and cellular senescence. Together, these processes reduce vascular flexibility, impair metabolism, and accelerate biological aging.

Among natural solutions, pomegranate (*Punica granatum* L.) has become a reference ingredient. Long celebrated in Mediterranean cultures as a symbol of vitality, its polyphenols, are known to counteract oxidative stress and support vascular and metabolic health. Within nutritional geroscience, pomegranate has become a model botanical for investigating natural interventions that counter inflammaging[1].

Pomanox®, Euromed's patented pomegranate extract, is manufactured using the proprietary Pure-Hydro Process®, a water-based, solvent-free extraction method. This process ensures the preservation of the fruit's complete polyphenol profile in a consistent and reproducible format, providing standardized concentrations of punicalagin and ellagic acid, the primary ellagitannins found in pomegranate. Punicalagins deliver sustained antioxidant protection and vascular support, while ellagic acid modulates cellular redox and detoxification pathways.

The HPLC profile of Pomanox® mirrors the fruit's native phenolic composition, ensuring that the extract retains the natural synergy of its precursors and provides the ideal substrate for physiological transformation through digestion.

During digestion, these compounds are converted by gut microbes into urolithins, bioavailable metabolites that promote mitochondrial renewal and cellular energy efficiency.

Supported by robust clinical and preclinical research, Pomanox® targets aging at various biological levels. From endothelial nitric-oxide restoration and IGF-1 balance to oxidative-stress defense and collagen renewal, research connects


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Pomanox® with multiple hallmarks of aging, supporting healthspan, vitality, and beauty from within.

Preclinical research reveals how Pomanox® acts on several interconnected biological pathways that help the body adapt, repair, and stay balanced.

Preclinical Mechanisms

AHR, a longevity switch

Research by the MODUL_AHR group (University of Valencia) has identified the aryl hydrocarbon receptor (AHR) as a central regulator of stress adaptation and longevity across species. The AHR is a cytoplasmic receptor that, upon ligand binding, translocates to the nucleus to regulate gene expression. Acting as a homeostatic sensor, AHR detects environmental and metabolic stress and coordinates detoxification, antioxidant, and immune pathways.

When AHR activity declines with age, this regulatory balance is lost, leading to chronic inflammation, impaired metabolism, and tissue vulnerability[2].

Given its central role in maintaining resilience, Pomanox® was investigated as an AHR modulator. In *C. elegans* (a microscopic worm widely used in aging research), supplementation extended lifespan and motility through AHR-dependent mechanisms, while the same benefits disappeared entirely in AHR-deficient mutants.

In aged mice, pomegranate extract supplementation upregulated AHR pathway genes in the liver, the body's main detoxification organ, enhancing its ability to manage oxidative and xenobiotic stress.

The same landmark study revealed that in humans, centenarians maintain markedly higher expression of AHR, its co-activator ARNT, and the downstream targets CYP1B1 and NFE2L2 (Nrf2) compared with individuals of average longevity[3].

This sustained activity may partly explain the superior stress resistance and detoxification capacity characteristic of exceptional aging.

Collectively, these findings suggest that Pomanox® supports healthy aging by reinforcing AHR-mediated control of detoxification, antioxidant defense, and cellular repair, mechanisms that appear naturally preserved in centenarians.

Oxidative-stress defense, cerebellum and mitochondrial protection

Building on the AHR data, the Valencia team explored how Pomanox® affects oxidative stress and mitochondrial health in aged models.

In aged mice, six weeks of supplementation with Pomanox® reduced oxidative stress, restored antioxidant enzyme activity (SOD, CAT, GPx), and improved redox balance[4].

A longer four-month intervention confirmed these effects and showed improved motor coordination and a higher GSH/GSSG ratio, a key marker of cellular redox balance and protection of the cerebellum, where mitochondrial function and neuromuscular control were preserved[5].

These outcomes indicate that Pomanox® enhances mitochondrial efficiency and protects neural tissue, acting as a metabolic stabilizer that may delay frailty.

Supporting vascular flexibility

Beyond its cellular effects, Pomanox® shows pronounced vascular benefits, an essential determinant of systemic aging.

In a preclinical model using hypercholesterolemic pigs, 10 days of supplementation (625 mg/day; 200 mg punicalagins) restored coronary relaxation to healthy levels[6].

This was linked to increased Akt/eNOS phosphorylation, boosting nitric-oxide (NO) synthesis, together with decreased MCP-1, a key inflammatory chemokine.

Oxidative DNA damage fell by 50%, while HDL antioxidant capacity rose and LDL oxidation lag time doubled.

These results align with upstream AHR and Nrf2 activation, demonstrating that Pomanox® simultaneously restores NO signaling and limits oxidative stress, re-establishing the redox-vascular balance often lost with age.

Metabolic and Microbiome Protection

In fructose-fed Wistar rats, Pomanox® (0.2% w/v) prevented:

- hepatic steatosis and glycoxidative stress
- visceral and subcutaneous fat accumulation
- dyslipidemia, with improved liver enzyme profile
- microbiome dysbiosis, together with the appearance of an urolithin-like metabolite

These findings[7] show that Pomanox® stabilizes the gut–liver–mitochondria axis, mitigating oxidative and metabolic stress and supporting healthy microbial diversity.

By providing substrates for urolithin formation, the extract connects gut ecology with mitochondrial renewal, defining a metabolic hallmark of healthspan.

Across these studies, Pomanox® consistently activated the AHR, Nrf2, and Akt/eNOS pathways, strengthening detoxification, antioxidant protection, and vascular health.

By integrating these mechanisms, the extract acts as a multi-pathway modulator of resilience, laying the foundation for its clinically proven human benefits.

Human Evidence: From Short-Term Adaptation to Long-Term Balance

Cardiovascular and Stress Adaptation

The first two human trials explored how short-term supplementation with Pomanox® influences blood pressure, oxidative balance, and cortisol metabolism.

In a 4-week placebo-controlled study, Stockton et al. [8] reported that 750 mg/day of Pomanox® significantly reduced both systolic and diastolic blood pressure, lowered cortisol and the cortisol-to-cortisone ratio, and improved insulin sensitivity and quality-of-life scores.

Participants also reported greater energy and improved mood after just one month.

A second 4-week randomized study by Al-Dujaili et al.[9] confirmed and expanded these results. Healthy volunteers taking 730 mg/day of Pomanox® (≈ 210 mg punicalagins) experienced similar blood pressure reductions, lower salivary cortisol, and a decreased cortisol/cortisone ratio, indicating reduced 11β-HSD1 activity, an enzyme that regenerates active cortisol and tends to increase with stress and age.

Lean mass rose slightly, while antioxidant capacity (FRAP) and urinary total phenolics increased in parallel, confirming bioavailability and systemic antioxidant action.

Importantly, urolithin-A glucuronide was detected in urine, confirming active microbial conversion of ellagitannins into systemic metabolites.

These adaptive responses resemble those produced by exercise or caloric restriction, showing that Pomanox® can gently activate healthspan physiology.

Longer-Term Effects: Inflammaging, IGF-1, Cognitive Vitality, and Performance

The most extensive clinical evaluation of Pomanox® comes from a 12-week, randomized, double-blind, placebo-controlled study conducted at Manchester Metropolitan University, led by Dr Grace Farhat, providing a comprehensive validation of Pomanox®'s healthspan potential.

Adults aged 55–70 years received 740 mg of Pomanox® daily, and the findings were presented in three peer-reviewed papers[10-12] exploring inflammation and vascular health, endocrine balance, and cognition.

Inflammaging and vascular function

After twelve weeks, participants taking Pomanox® showed a significant reduction in pro-inflammatory cytokines, specifically interleukin-6 (IL-6) and interleukin-1β (IL-1β), both important factors in inflammaging. Although CRP and TNF-α decreased without reaching statistical significance, the overall pattern pointed to a clear attenuation of inflammaging.

Additionally, their systolic blood pressure decreased by roughly 5 mmHg (–5.2 ± 1.3 mmHg; $p = 0.04$), and there was also a downward trend observed in diastolic blood pressure (–2.94 ± 1.08 mmHg; $p = 0.3$). These findings indicate a measurable reduction of inflammaging, a condition that contributes to vascular stiffness and

metabolic dysfunction with age[10].

Clinically, a 5 mmHg reduction in systolic blood pressure translates to about a 10 percent lower risk of cardiovascular events, making this change meaningful even in healthy, non-hypertensive adults.

Together with the decline in inflammatory markers, these results show how Pomanox® can counter the biological friction of aging, maintaining circulatory efficiency and systemic homeostasis.

Restoring IGF-1 within the physiological range

One of the most distinctive findings of the Manchester trial was a moderate but significant increase in circulating IGF-1, about +14 ng/mL on average ($p = 0.04$), while remaining comfortably within normal values for age.

Importantly, there were no changes in IGF-binding proteins and no telomere shortening, confirming that the rise reflected balanced endocrine recovery rather than stimulation[11].

IGF-1, the insulin-like growth factor, plays a central role in maintaining muscle tone, vascular elasticity, and tissue repair. Its levels typically decline with age, contributing to frailty and slower recovery from daily stress.

By restoring IGF-1 toward mid-range levels, Pomanox® appears to reactivate the body's natural repair pathways, supporting anabolic functions without disrupting metabolic control.

This restoration of anabolic balance (hormonal homeostasis) occurred alongside the reduction of IL-6 and IL-1β, illustrating how inflammatory and regenerative signals are interconnected: as cytokine activity decreases, the GH/IGF-1 axis functions more efficiently.

While telomere length did not change within the twelve-week timeframe, this stability itself confirms genomic safety and suggests that with longer interventions, improved redox and endocrine balance may help preserve telomere integrity over time.

Cognitive benefits

Participants taking Pomanox® made 20% fewer errors in the Wisconsin Card Sorting Test ($p = 0.05$), reflecting sharper executive function and mental flexibility, with trends toward improved memory and inhibitory control[12].

Better nitric-oxide activity and mitochondrial performance likely underlie these results, improving cerebral blood flow and neuronal energy.

Earlier acute data support this connection: in a double-blind crossover study[13], a single dose of 1,400 mg Pomanox® (420 mg punicalagins) enhanced reaction time, attention, and memory accuracy within one hour ($p < 0.05$).

Together, these trials demonstrate both immediate and sustained cognitive support, from rapid improvements in focus to long-term enhancement of executive performance.

Performance and Recovery

The same physiological pattern appears in physical performance and sports recovery.

In trained cyclists, 15 days of supplementation (225 mg punicalagins/day) increased time-to-exhaustion by 170 seconds ($p < 0.02$) and reduced C-reactive protein (CRP) and creatine kinase (CK) levels after exercise.

This shows faster recovery, reduced inflammation, and more efficient oxygen use[14]. By promoting endurance and repair, Pomanox® extends its benefits from the lab to real-world physical performance, bridging active living and longevity.


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Skin Health and Beauty from Within

Beyond systemic benefits, Pomanox®'s biological harmony also translates into visible improvements in skin vitality.

Research at the Eurecat Technology Center shows[15] that Pomanox® promotes dermal renewal and photoprotection in human fibroblasts (Hs68).

The extract increased type I collagen and total collagen, reduced MMP-1, boosted hyaluronic acid synthesis, lowered ROS formation under UV-B, and inhibited tyrosinase activity ($IC_{50} \approx 395\ \mu g/mL$).

By modulating the same AHR–Nrf2–Akt/eNOS–IGF network active in systemic tissues, Pomanox® enhances extracellular matrix integrity, hydration, and microcirculation. Preliminary data from a large clinical study suggest improvements in skin biomarkers and microbiome balance, demonstrating that Pomanox® supports both longevity and aesthetic health[16].

Connecting the Dots: The Longevity Network

Across all studies, the picture is consistent: Pomanox® supports a network of biological pathways that maintain equilibrium.

At the cellular level, it activates AHR and Nrf2, the master regulators of detoxification and antioxidant defense.

In the circulation, it improves Akt/eNOS signaling and nitric-oxide release, keeping blood vessels flexible.

At the hormonal level, it restores IGF-1 within a healthy range, reinforcing tissue repair.

Through the microbiome, it promotes the formation of urolithins, connecting gut health to mitochondrial renewal.

Each mechanism may amplify the others, creating a self-reinforcing system of detoxification, protection, and regeneration.

Rather than stimulating the body, Pomanox® helps it respond more efficiently to daily stress, a physiological balance that mirrors the effects of regular exercise or a Mediterranean diet.

From Mechanism to Market

Behind the science is Euromed's long-term commitment to quality and sustainability.

Pomanox® is made from Mediterranean pomegranates using the Pure-Hydro Process®, an eco-friendly, solvent-free extraction method that preserves the fruit's natural spectrum of polyphenols while minimizing environmental impact.

The extract is manufactured under Euromed's PhytoProof® quality program, ensuring full traceability, identity, and reproducibility.

Its composition mirrors the whole fruit but in a form that is easy to formulate into dietary supplements, functional foods, and beverages.

Because it is water-soluble and has a pleasant taste, it fits naturally into new formats such as gummies, ready-to-drink shots, and plant-based blends.

Conclusion

Across mechanistic, preclinical, and clinical studies, Pomanox® harmonizes the molecular networks that sustain healthy longevity. By activating the AHR–Nrf2–Akt/eNOS–IGF axis, reducing inflammation, restoring vascular and metabolic balance, and protecting dermal and neuronal tissues, it defines a new paradigm of integrative rejuvenation.

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