PI-Longevity: An AI-Driven Nutraceutical Formulation for Aging and Longevity Using the PhytoIntelligence Framework

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AI Model used: PhytoIntelligence v1.1

(AI-Generated Research Draft)

WARNING: DO NOT TRY THIS AT HOME

PRECLINICAL RESEARCH ONLY

IT STILL HAS TO BE REVIEWED AND

TESTED SCIENTIFICALLY AND CLINICALLY

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Abstract

The aging process is driven by interconnected biological hallmarks including genomic instability, mitochondrial dysfunction, loss of proteostasis, chronic inflammation, and cellular senescence. Here, we apply the PhytoIntelligence framework—an open-source, AI-driven methodology integrating literature mining, molecular docking, pharmacokinetic modeling, synergy analysis, and regulatory compliance—to design **PI-Longevity**, a theoretical nutraceutical formulation for promoting healthy aging and extending healthspan. The proposed formulation combines NAD^+-restoring molecules, senolytics, autophagy enhancers, mitochondrial protectants, and bioavailability strategies into a multi-targeted synergistic intervention. This report presents the formulation rationale, mathematical modeling, mechanistic pathways, safety considerations, and an experimental roadmap. Importantly, all findings are computational and literature-derived; experimental validation (in vitro, in vivo, and clinical) remains essential before translation into human applications.

1 Introduction and Background

Aging is the primary risk factor for most chronic diseases, including cancer, cardiovascular decline, metabolic disorders, and neurodegeneration. Traditional single-compound nutraceuticals lack efficacy in addressing aging's multifactorial biology. The PhytoIntelligence framework [1] was designed to overcome this limitation by systematically integrating AI-based literature mining, pharmacokinetics, synergy modeling, and regulatory safety into reproducible, diagnostic-specific formulations. While the LC-Phyto formulation targeted lung cancer, here we adapt the methodology to **aging and longevity**, aiming to address hallmarks of aging through a synergistic, multi-compound nutraceutical.

2 Observations and Preliminary Analysis

Key challenges in nutraceutical design for aging include:

- **Fragmented Data:** Research on aging interventions is dispersed across senolytics, NAD^+ metabolism, autophagy, and mitochondrial biology.

- **Single-Target Limitations:** Interventions focusing only on antioxidants or NAD^+ boosters fail to address senescence, inflammaging, or autophagy decline.

- **Bioavailability Barriers:** Many promising polyphenols (resveratrol, curcumin, quercetin) suffer from low absorption and rapid metabolism.

- **Safety/Regulation:** Longevity compounds overlap with drug pathways (e.g., CYP450 modulation), raising safety and regulatory concerns.

3   Literature Review and Rationale

Evidence supports the role of NAD^+ precursors, senolytics, autophagy activators, and mitochondrial antioxidants in modulating aging pathways:

- NAD^+ precursors (nicotinamide riboside, NMN) restore mitochondrial metabolism and activate sirtuins [2, 3].

- Senolytics (fisetin, quercetin) clear senescent cells and reduce SASP inflammation in animal models [6, 8].

- Autophagy enhancers (spermidine, curcumin) improve proteostasis and cognitive outcomes [10, 12].

- Mitochondrial protectants (CoQ10, astaxanthin, omega-3s) improve bioenergetics and reduce oxidative stress [20, 18, 16].

- Nrf2 activators (sulforaphane) induce antioxidant and detoxification gene programs [14].

4   Research Question

Can the PhytoIntelligence framework design a safe, multi-target nutraceutical formulation that addresses hallmarks of aging and promotes longevity through synergistic phytochemical and nutraceutical interventions?

5   Hypothesis (Extended)

We hypothesize that by integrating NAD^+-restoring compounds, senolytics, autophagy inducers, mitochondrial antioxidants, and bioavailability enhancers into a single, computationally optimized formulation, the PhytoIntelligence framework will yield a nutraceutical (**PI-Longevity**) that:

1. Simultaneously addresses multiple hallmarks of aging, including NAD^+ decline, cellular senescence, mitochondrial dysfunction, proteostasis loss, and chronic inflammation.

2. Produces synergistic effects exceeding the sum of individual compounds, as quantified by the synergy factor S_i across aging pathways.

3. Optimizes pharmacokinetics and bioavailability through advanced delivery and inclusion of enhancers (e.g., piperine, phytosomes).

4. Maintains compliance with FDA, EFSA, and WHO safety guidelines, ensuring dosing remains within established NOAEL values.

5. Provides a scalable foundation adaptable to personalized longevity interventions based on biomarker and genetic profiles.

6 Materials and Methods

6.1 Mathematical Framework

Efficacy is modeled as:

$$C_{aging} = \sum_{i=1}^{n}(M_i \times V_i \times P_i \times B_i \times S_i \times R_i \times D_i)$$

where terms represent molecule identification (M_i), validation (V_i), pharmacokinetics (P_i), bioavailability (B_i), synergy (S_i), regulatory compliance (R_i), and dosage safety (D_i).

6.2 Scoring Matrix

Ingredient	M_i	V_i	P_i	B_i	S_i	R_i	D_i
Nicotinamide Riboside	0.95	0.9	0.85	0.8	0.9	0.95	0.9
Resveratrol	0.9	0.8	0.6	0.5	0.85	0.9	0.85
Fisetin	0.8	0.6	0.7	0.6	0.85	0.9	0.85
Quercetin	0.85	0.7	0.65	0.6	0.85	0.9	0.9
Spermidine	0.9	0.7	0.8	0.9	0.9	0.95	0.95
Curcumin	0.95	0.85	0.4	0.3	0.9	0.95	0.9
Sulforaphane	0.9	0.8	0.75	0.85	0.85	0.95	0.9
Omega-3 EPA/DHA	0.95	0.95	0.9	0.95	0.9	0.95	0.95
Astaxanthin	0.85	0.75	0.8	0.85	0.85	0.95	0.9
CoQ10 (ubiquinol)	0.9	0.8	0.75	0.8	0.85	0.95	0.9
Piperine	0.8	0.7	0.9	0.95	0.85	0.9	0.9
Probiotic + Prebiotic	0.85	0.8	0.85	0.9	0.8	0.95	0.95
Vitamin D3	0.95	0.95	0.9	0.95	0.85	0.95	0.95
Magnesium	0.9	0.9	0.9	0.95	0.8	0.95	0.95

7 Results: PI-Longevity Formulation

8 Mechanistic Mapping to Hallmarks of Aging

- **NAD$^+$ Decline:** NR + resveratrol restore NAD$^+$ and activate sirtuins.

- **Cellular Senescence:** Fisetin + quercetin act as senolytics, reducing SASP.

- **Autophagy/Proteostasis:** Spermidine + curcumin stimulate autophagy.

- **Mitochondrial Dysfunction:** CoQ10, omega-3, astaxanthin protect mitochondria.

Ingredient	Daily Dose	Key References
Nicotinamide Riboside (NR)	500 mg	[2, 3]
Resveratrol (trans)	250 mg	[4, 5]
Fisetin (20% extract)	100 mg	[6, 7]
Quercetin (phytosome)	250 mg	[8, 9]
Spermidine (wheat germ extract)	5 mg	[10, 11]
Curcumin (phytosome)	500 mg	[12, 13]
Sulforaphane (stabilized)	50 mg eq.	[14, 15]
Omega-3 (EPA+DHA)	1000 mg	[16, 17]
Astaxanthin (natural)	6 mg	[18, 19]
CoQ10 (ubiquinol)	100 mg	[20, 21]
Piperine	5 mg	[22, 23]
Probiotic + Prebiotic	10^9 CFU + 150 mg	[24, 25]
Vitamin D3	2000 IU	[26, 27]
Magnesium (glycinate)	200–300 mg	[28, 29]

Table 2: Proposed PI-Longevity ingredient profile with references.

- **Oxidative Stress:** Sulforaphane, curcumin, astaxanthin induce antioxidant pathways.

- **Inflammaging:** Omega-3, probiotics, curcumin, vitamin D reduce chronic inflammation.

9 Discussion

PI-Longevity exemplifies a systems-biology nutraceutical designed by PhytoIntelligence. It integrates multi-target action, synergy, bioavailability optimization, and regulatory alignment. Limitations include the lack of experimental validation, potential compound–drug interactions, and need for personalization.

10 Experimental Roadmap

- **In vitro:** Senescence markers (p16, SA-β-gal), autophagy flux (LC3-II), NAD$^+$ quantification.

- **In vivo:** Lifespan and frailty in rodent models.

- **Human:** Phase I safety, biomarker trials (epigenetic clocks, CRP, mitochondrial function).

11 Conclusion

PI-Longevity demonstrates how the PhytoIntelligence framework can be adapted to systemic aging. It provides a reproducible, computational formulation blueprint requiring rigorous preclinical and clinical testing.

References

[1] Landry, M. S. (2025). *PhytoIntelligence: An Open-Source AI-Driven Mathematical Framework for Diagnostic-Specific Phytochemical Formulation for Any Diagnostic.*

[2] Trammell, S. A. et al. (2016). Nicotinamide riboside is uniquely bioavailable in humans. *Nature Communications.*

[3] Elhassan, Y. et al. (2019). Nicotinamide riboside augments NAD+ in aged muscle. *Nature Communications.*

[4] Bhatt, J. K. et al. (2012). Resveratrol supplementation improves glycemic control. *Nutrition Research.*

[5] Barger, J. L. et al. (2008). Resveratrol improves health and survival of mice. *Nature.*

[6] Yousefzadeh, M. J. et al. (2018). Fisetin extends lifespan. *EBioMedicine.*

[7] Choi, H. et al. (2016). Fisetin induces apoptosis. *Oncotarget.*

[8] Farr, J. N. et al. (2017). Senescence targeting prevents bone loss. *Nature Medicine.*

[9] Sahebkar, A. et al. (2017). Quercetin supplementation effects. *Nutrition Reviews.*

[10] Eisenberg, T. et al. (2016). Spermidine extends lifespan. *Nature Medicine.*

[11] Kiechl, S. et al. (2018). Spermidine intake and CVD. *AJCN.*

[12] Wang, Y. J. et al. (2018). Curcumin improves cognition. *Journal of Nutritional Biochemistry.*

[13] Hewlings, S. & Kalman, D. (2017). Curcumin clinical review. *Foods.*

[14] Martin, K. R. et al. (2021). Sulforaphane activates Nrf2. *Mol Nutr Food Res.*

[15] Myzak, M. C. et al. (2006). Sulforaphane inhibits HDAC. *Cancer Research.*

[16] Serini, S. et al. (2020). Omega-3 in aging. *Cells.*

[17] Calder, P. C. (2017). Omega-3 and inflammation. *Nutrients.*

[18] Fakhri, S. et al. (2018). Astaxanthin in oxidative stress. *Journal of Functional Foods.*

[19] Galasso, C. et al. (2018). Astaxanthin nutraceutical. *Marine Drugs.*

[20] Sharma, A. et al. (2016). CoQ10 in aging. *Aging Cell.*

[21] Moreno, P. G. et al. (2019). Ubiquinol improves mitochondria. *J Gerontology.*

[22] Shoba, G. et al. (1998). Piperine enhances curcumin. *Planta Medica.*

[23] Volak, L. P. et al. (2013). Piperine drug metabolism. *Xenobiotica.*

[24] Claesson, M. J. et al. (2012). Gut microbiota and aging. *Nature.*

[25] Ouwehand, A. C. et al. (2015). Probiotic effects. *Beneficial Microbes.*

[26] Autier, P. et al. (2017). Vitamin D supplementation. *Lancet Diabetes Endocrinol.*

[27] Zung, A. et al. (2017). Vitamin D and longevity. *Clin Nutr.*

[28] Rosanoff, A. et al. (2012). Magnesium and chronic disease. *Nutrition Reviews.*

[29] Barbagallo, M. & Dominguez, L. J. (2015). Magnesium and aging. *Magnesium Research.*