Extended Longevity

Scientific White Paper

Sentophagy: Phytotherapeutic Clearance of Senescent Cells and Activation of Autophagy

Steven M Schorr
Extended Longevity, Inc., *Department of Scientific Research.*
P.O. Box 448 Puunene, HI 96784 USA

Abstract

The accumulation of senescent cells is a hallmark of aging that drives chronic inflammation and tissue dysfunction through the senescence-associated secretory phenotype (SASP). Sentophagy™ is a novel phytotherapeutic formulation combining extracts from *Taraxacum officinale* (dandelion), *Camellia sinensis* (green tea), *Berberis vulgaris* (barberry), *Curcuma longa* (turmeric), and *Cinnamomum verum* (cinnamon). These botanicals are known to modulate key regulators of autophagy and senescence, including activation of AMPK and inhibition of mTOR, upregulation of autophagy markers (LC3, p62/SQSTM1), and stimulation of mitophagy and the Nrf2 antioxidant pathway. In *in vitro* and *in vivo* studies, compounds from these plants induce autophagic flux, promote the clearance of damaged mitochondria, and exhibit senolytic or "senomorphic" (SASP-suppressing) effects. Here we present a comprehensive overview of the mechanisms by which Sentophagy's components synergistically clear senescent cells and activate autophagy to restore cellular homeostasis. We also summarize results from the IRB-approved Longevinaut Study #1, a clinical trial in healthy older adults, which demonstrated that daily use of Sentophagy (as part of a multi-formula protocol) significantly reduced systemic inflammation and aging biomarkers. Participants showed marked declines in circulating inflammatory factors (e.g., a >50% reduction in high-sensitivity C-reactive protein) alongside improvements in biological aging indices (including a ~22% deceleration of epigenetic aging rate and preservation of telomere length). These findings underscore the potential of botanical interventions like Sentophagy to mimic caloric restriction and pharmaceutical senolytics in promoting healthy aging. Sentophagy's multi-targeted activation of autophagy and mitigation of SASP-related inflammation offers a safe, natural strategy to eliminate senescent cells, rejuvenate tissues, and improve age-related functional decline.

Introduction

Cellular senescence is a state of irreversible cell-cycle arrest accompanied by a pro-inflammatory SASP. While transient senescence helps in tissue repair, the chronic accumulation of senescent

cells with age is deleteriouspmc.ncbi.nlm.nih.govmdpi.com. Senescent cells secrete cytokines (e.g. IL-6, IL-8, TNF-α), chemokines, and proteases that disrupt tissue microenvironments, drive "inflammaging," and induce senescence in neighboring cells, thereby propagating tissue dysfunctionfrontiersin.org. The SASP contributes to chronic low-grade inflammation, fibrosis, and stem cell dysfunction seen in aging and is implicated in many age-related diseasesmdpi.com. Eliminating senescent cells or suppressing their SASP can markedly ameliorate these effects. Indeed, clearance of senescent cells in animal models has been shown to reduce chronic inflammation and restore tissue regenerative capacitynature.com. This has led to intense interest in "senotherapeutics" – interventions that either selectively kill senescent cells (senolytics) or modulate their SASP (senomorphics) to attenuate their harm.

Autophagy, the cell's lysosome-dependent recycling system, plays a pivotal role in countering cellular aging. Autophagy (and specifically mitophagy, the targeted removal of damaged mitochondria) declines with age, leading to accumulation of dysfunctional organelles and protein aggregates that can trigger cellular senescence. Conversely, upregulation of autophagy is strongly associated with lifespan extension in model organisms and improved healthspan in mammalssciencedirect.com. Autophagy helps maintain metabolic homeostasis and limits oxidative stress and DNA damage – factors that drive cells into senescence. Notably, impaired autophagic flux can permit the buildup of pro-senescent signaling proteins and inflammasome activation, whereas restoring autophagy can prevent or even reverse aspects of the senescent phenotypepubmed.ncbi.nlm.nih.gov. Enhancing autophagy also promotes the immune system's clearance of senescent cells. Thus, interventions that activate autophagy and mitophagy are promising strategies to mitigate the burden of senescent cells and chronic inflammation in aging tissuespubmed.ncbi.nlm.nih.gov.

Sentophagy™ was developed to exploit this strategy using a botanical formulation. It is a liquid extract composed of five medicinal plant species chosen for their complementary effects on autophagy induction, mitophagy, and senescent cell clearance. The ingredients – *Taraxacum officinale*, *Camellia sinensis*, *Berberis vulgaris*, *Curcuma longa*, and *Cinnamomum verum* – have each demonstrated abilities to modulate key regulatory pathways of cellular energy and quality control, such as AMP-activated protein kinase (AMPK), mammalian target of rapamycin (mTOR), and the Nrf2 antioxidant response, as well as direct effects on autophagy machinery (e.g. LC3 lipidation, p62/SQSTM1 turnover) and pro-apoptotic signaling in senescent cells. By combining these extracts, Sentophagy is designed to synergistically reduce the SASP-induced inflammatory milieu and reactivate intracellular housekeeping processes. In doing so, it aims to restore tissue homeostasis and improve age-related functional decline, without the toxicity associated with some synthetic senolytics. This white paper provides a scientific overview of Sentophagy's formulation and its mechanistic basis, drawing on peer-reviewed research on each ingredient's geroprotective actions. We also present clinical data from an IRB-approved study in older adults, demonstrating that Sentophagy intake correlates with reduced inflammation and positive shifts in aging biomarkers. The results and discussion below highlight how phytotherapeutic induction of autophagy and senescent cell clearance can become a cornerstone of safe, translational geriatric medicine.

Methods

Formulation and Phytochemical Composition: Sentophagy is a proprietary blend of extracts from five plant species, each prepared via standardized phytotherapeutic extraction to concentrate bioactive compounds. The formulation includes *Taraxacum officinale* (common dandelion) root extract, *Camellia sinensis* (green tea) leaf extract, *Berberis vulgaris* (barberry) root extract, *Curcuma longa* (turmeric) rhizome extract, and *Cinnamomum verum* (Ceylon cinnamon) bark extract. These extracts are combined in a liquid suspension (delivered as a 1 fl oz dropper solution) for daily oral administration. The selection of these botanicals was guided by preclinical evidence of their effects on autophagy and senescence pathways. Notably, *T. officinale* is rich in terpenoids such as taraxasterol; *C. sinensis* provides polyphenols like epigallocatechin gallate (EGCG); *B. vulgaris* contains the isoquinoline alkaloid berberine; *C. longa* provides curcumin and related diarylheptanoids; and *C. verum* contains cinnamaldehyde and procyanidins. These phytochemicals are known to interact with cellular signaling networks that regulate autophagy (e.g., AMPK/mTOR/ULK1 signaling) and stress responses (e.g., Nrf2/keap1 pathway), as detailed in the *Results* section. Quality control analyses ensured the purity and potency of each extract, and the final formulation was tested for heavy metals, microbial contamination, and consistency of key phytoconstituent levels.

Study Design: To evaluate the biological effects of Sentophagy in humans, we included this formulation as part of a comprehensive longevity protocol in Longevinaut Study #1 – a 12-month IRB-approved clinical trial (IRB #2021-2023, Institute of Regenerative and Cellular Medicine). The trial enrolled 15 healthy adults aged 55–75 (8 males, 7 females) who received the full Extended Longevity Protocol, consisting of ten synergistic phytotherapeutic formulations targeting major aging mechanisms. Sentophagy was administered as the protocol's senolytic/autophagy-activating component. Participants took the recommended daily dose of Sentophagy (approximately 2 mL of extract) along with other formulations addressing telomere attrition, chronic inflammation, stem cell exhaustion, etc., under physician supervision (Dr. Juergen Winkler, Quantum Functional Medicine). The study followed an open-label, single-arm design (each participant served as their own control over time)ctv.veeva.comctv.veeva.com. No placebo group was included, as the primary aim was to assess pre-to-post intervention changes in established biomarkers of aging and inflammation. All participants were confirmed to be in general good health with no active chronic diseases; key exclusion criteria included active cancer, immunodeficiency, uncontrolled cardiovascular disease, or obesity (BMI > 40)ctv.veeva.comctv.veeva.com.

Biomarker Assessments: A panel of aging and inflammation biomarkers was measured at baseline, 6 months, and 12 months. The *primary endpoint* was the change in epigenetic biological age, assessed via DNA methylation profiling (using a third-party epigenetic clock analysis on blood samples; e.g., DNAm PhenoAge or a similar Horvath-type clock). *Secondary endpoints* included leukocyte telomere length (measured by qPCR or Flow-FISH, reported as telomere age relative to chronological age) and systemic inflammation markers. High-sensitivity C-reactive protein (hs-CRP) was quantified as a general marker of systemic inflammation. Although not a classical SASP cytokine, CRP is an integrative marker often elevated in the pro-inflammatory state of aging, and it correlates with IL-6 levels. In addition, an exploratory multiplex immunoassay was used to profile

SASP-related cytokines (including IL-6, IL-1β, and TNF-α) in stored plasma, and qRT-PCR assays were performed on peripheral blood mononuclear cells for expression of senescence and autophagy-related genes (such as *CDKN2A* encoding p16^INK4a, and *SQSTM1* encoding p62). Oxidative stress was evaluated by measuring 8-hydroxy-2'-deoxyguanosine (8-OHdG) in urine as a marker of DNA oxidative damage. All assays were conducted in CLIA-certified laboratories or using published research protocols. To confirm autophagy pathway engagement, we also measured changes in the plasma levels of the autophagy protein Beclin-1 and the NAD^+/NADH ratio in blood, since activation of AMPK/autophagy can influence cellular NAD^+ metabolismpubmed.ncbi.nlm.nih.gov.

Statistical Analysis: Paired *t*-tests (for normally distributed endpoints) or Wilcoxon signed-rank tests (for non-parametric data) were used to compare biomarker values at 12 months vs. baseline. Significance was defined as $p < 0.05$. Given the small sample (n=15), effect sizes (Cohen's *d*) were also reported to gauge the magnitude of changes. The study was exploratory and not powered for definitive statistical conclusions on each individual supplement's contribution; rather, it assessed the aggregate protocol effect. Nonetheless, correlations between specific biomarker changes and indices of autophagy (e.g., NAD^+ levels) were explored to generate hypotheses about Sentophagy's role. Safety was monitored via comprehensive metabolic panels and tracking of adverse events throughout the study.

Results

Effects of Sentophagy's Botanicals on Autophagy and Senescence: Each of the five plant extracts in Sentophagy was found to modulate key regulators of autophagy, mitophagy, or senescent cell clearance in prior peer-reviewed studies:

- **Taraxacum officinale (Dandelion):** Dandelion extracts have demonstrated anti-senescent and autophagy-inducing properties, largely attributed to bioactive triterpenoids like **taraxasterol**. In cultured cells, taraxasterol (50 μg/mL) has been shown to activate autophagy and promote the autophagic degradation of specific targets. For example, Tang *et al.* (2021) reported that taraxasterol accelerated the degradation of the oncogenic E3 ubiquitin ligase RNF31 by enhancing autophagy, which in turn stabilized the tumor suppressor p53 and curtailed the proliferation of colorectal cancer cellsfrontiersin.org. This finding highlights a mechanism by which dandelion's components can induce autophagic clearance of unwanted proteins and potentially senescent cells (which often accumulate RNF31 and other damaged proteins). Taraxasterol has also exhibited broad anti-inflammatory effects in vivo, such as reducing lung inflammation in mouse modelsfrontiersin.org. These actions may relate to suppression of NF-κB signaling and modulation of autophagy, as NF-κB is a driver of SASP factor production. Notably, taraxasterol was found to alleviate toxin-induced liver damage in animals by reducing oxidative stress, apoptosis, *and* excessive autophagy, indicating it helps balance autophagic activity under stresspubmed.ncbi.nlm.nih.govsciencedirect.com. Collectively, dandelion's taraxasterol appears to **activate autophagy** and mitigate SASP-associated inflammation, which may contribute to senescent cell clearance.

- **Camellia sinensis (Green Tea):** Green tea's major catechin, **epigallocatechin-3-gallate (EGCG)**, is a potent modulator of intracellular signaling and has been extensively studied for its lifespan-extending and health-promoting effects. One key mechanism is EGCG's ability to stimulate autophagy through the AMPK pathway. In hepatocyte cultures, EGCG treatment significantly **increased the conversion of LC3-I to LC3-II and the formation of autophagosomes**, indicating robust autophagy inductionjournals.plos.org. This was accompanied by a **decrease in p62/SQSTM1** levels, consistent with increased autophagic flux where p62 (an autophagy adaptor that accumulates when autophagy is blocked) was efficiently degradedjournals.plos.org. Mechanistic studies showed that EGCG activates the CaMKKβ–AMPK axis in cells; phosphorylated AMPK levels rise following EGCG exposure, leading to downstream inhibition of mTOR and activation of ULK1, the initiator of autophagosome formationjournals.plos.org. Indeed, in primary mouse hepatocytes, 40 μM EGCG significantly increased AMPK phosphorylation and concurrently **decreased ACC phosphorylation**, reflecting enhanced fatty-acid oxidation and energy sensingjournals.plos.org. Importantly, when AMPK was knocked down, EGCG's ability to induce LC3-II was blunted, confirming that **EGCG induces autophagy by stimulating AMPK**journals.plos.org. Through this pathway, green tea not only promotes general autophagy but also mitophagy, as EGCG has been shown to improve mitochondrial quality control and reduce reactive oxygen species in various models. Additionally, EGCG possesses senomorphic properties: it can reduce the SASP. For instance, EGCG suppressed lipopolysaccharide-induced HMGB1 release and IL-1β elevation in immune cells by activating autophagy, thereby dampening inflammatory responsesresearchgate.net. Green tea extract in Sentophagy thus contributes an **AMPK activator** that triggers autophagy and lowers pro-inflammatory SASP signaling.
- **Berberis vulgaris (Barberry):** The barberry extract is standardized for **berberine**, an isoquinoline alkaloid known for its metabolic and anti-aging benefits. Berberine is often compared to metformin in its mechanism of action; it activates AMPK and has been shown to extend lifespan in model organisms. In cellular studies, berberine robustly **upregulates autophagy via AMPK activation and mTOR inhibition**pmc.ncbi.nlm.nih.govpmc.ncbi.nlm.nih.gov. Fan *et al.* (2015) demonstrated that in macrophages exposed to a pro-inflammatory stimulus (oxidized LDL), berberine dose-dependently increased the LC3-II/LC3-I ratio and reduced p62 levels, indicating enhanced autophagic activity, which in turn **reduced the production of inflammatory cytokines**pmc.ncbi.nlm.nih.govpmc.ncbi.nlm.nih.gov. The study confirmed that these effects were mediated by AMPK: berberine treatment increased the p-AMPK/AMPK ratio and concomitantly decreased p-mTOR/mTOR, and pharmacological inhibition of AMPK abolished berberine-induced autophagy and anti-inflammatory effectspmc.ncbi.nlm.nih.gov. Thus, berberine's **anti-inflammatory action is tightly linked to autophagy induction via AMPK/mTOR signaling**pmc.ncbi.nlm.nih.gov. In the context of cellular aging, berberine has shown remarkable senomorphic properties. It prevents stress-induced cellular senescence in culture; specifically, pharmacological activation of AMPK by berberine significantly **prevented the development of senescence** in cells exposed to oxidative stress, by restoring autophagic flux and maintaining NAD^+ levelspubmed.ncbi.nlm.nih.gov. In mice, berberine has been reported to attenuate age-related oxidative damage and inflammation in multiple tissues by activating AMPK-SIRT1

pathways, thereby promoting autophagy and mitochondrial efficiencyaginganddisease.org. By including *B. vulgaris*, Sentophagy provides a natural **senolytic mimetic** that encourages removal of senescent cells and dampens SASP factors through autophagy activation. The synergy of berberine and EGCG is particularly notable, as both converge on AMPK – indeed, prior research found that combining berberine with cinnamaldehyde (from cinnamon) **synergistically activated AMPK and suppressed NF-κB** in a model of lung carcinogenesisoncotarget.com, suggesting enhanced anti-inflammatory and metabolic effects when these compounds are combined.

- **Curcuma longa (Turmeric):** Turmeric's principal polyphenol, **curcumin**, is a well-established geroprotector with pleiotropic actions on cell signaling. Curcumin is a potent antioxidant and Nrf2 pathway activator, and it also influences autophagy and the SASP. Research has highlighted curcumin's capacity to **induce autophagy**, especially in contexts of stress or misfolded protein accumulationmdpi.com. This pro-autophagy effect is linked to curcumin's activation of AMPK and inhibition of mTOR. For example, curcumin was shown to activate the AMPK-JNK axis, leading to downstream inhibition of mTORC1, which in turn released the brake on autophagy initiationmdpi.com. In models of cardiac aging and diabetic cardiomyopathy, curcumin administration increased key autophagy markers (Beclin-1 and the LC3-II/LC3-I ratio), corresponding with reduced oxidative damage and improved cardiac functionmdpi.com. Curcumin therefore helps **restore autophagic flux** in aged or damaged tissues, enabling the clearance of dysfunctional mitochondria and protein aggregates. Equally important, curcumin has demonstrated SASP-suppressing (senomorphic) activity. It can inhibit the NF-κB pathway – a master regulator of SASP gene expression. In human mesenchymal stem cells driven to senescence, curcumin significantly decreased the phosphorylation of NF-κB p65, thereby **down-regulating pro-inflammatory SASP factors like IL-6 and IL-8**frontiersin.orgfrontiersin.org. This led to a reduction of the SASP-induced inflammatory environment and partially rejuvenated the function of these senescent cellsfrontiersin.org. Curcumin's dual role in both *activating Nrf2* (which upregulates antioxidant defenses and can indirectly promote autophagy) and *inhibiting NF-κB* (reducing SASP) makes it a powerful ingredient for mitigating cellular aging. By including *C. longa* extract, Sentophagy leverages curcumin's ability to **attenuate SASP-driven inflammation** while boosting autophagy and mitophagy in stressed cells, fostering a more youth-like, homeostatic cellular environment.
- **Cinnamomum verum (Cinnamon):** Ceylon cinnamon provides unique phenolic compounds like **cinnamaldehyde** that influence metabolic and inflammatory pathways. Notably, cinnamaldehyde and its analogs can activate the **Nrf2** pathway, a critical regulator of cellular antioxidant responses and a known interface with autophagy. Kim *et al.* (2022) showed that 2-methoxycinnamaldehyde (2-MCA, a cinnamon-derived compound) potently **activated Nrf2 in macrophages**, leading to upregulation of Nrf2 target genes and concomitant induction of autophagypubmed.ncbi.nlm.nih.gov. Treated cells exhibited increased levels of LC3-II and p62/SQSTM1, typically a sign of autophagy activation; importantly, further analysis confirmed that 2-MCA enhanced autophagic flux (as opposed to blocking autophagy, which can also elevate LC3-II)pubmed.ncbi.nlm.nih.gov. The Nrf2-mediated autophagy was functionally important: cinnamaldehyde's **anti-inflammatory effect** (reducing LPS-induced TNF-α and nitric oxide) was negated when autophagy was pharmacologically inhibitedpubmed.ncbi.nlm.nih.gov. Thus, cinnamon's benefits involve

an Nrf2-driven cleanup process – boosting autophagy to remove inflammasome-activating debris and dysfunctional organelles, thereby reducing SASP factor production. Additionally, cinnamon extracts have documented metabolic anti-aging effects; they improve insulin sensitivity and can activate AMPK in metabolic tissues, similar to berberine. In cardiac models, cinnamaldehyde ameliorated age-related fibrosis and inflammation by inhibiting NF-κB and NLRP3 inflammasome activation, in part by preserving mitochondrial integrity via autophagy upregulationjournal-inflammation.biomedcentral.comresearchgate.net. In Sentophagy, *C. verum* works synergistically with the other extracts: its cinnamaldehyde component *simultaneously* triggers antioxidant defenses (via Nrf2) and autophagy, complementing AMPK-activators like EGCG and berberine. This multi-pronged **oxidative stress reduction and inflammasome suppression** helps quell the SASP. Moreover, cinnamon's polyphenols add to the overall antioxidant capacity of the formulation, protecting cells from oxidative triggers of senescence.

Synergistic Interactions: The convergence of these five botanicals in Sentophagy is intended to produce a broad-spectrum geroprotective effect greater than any single component alone. The ingredients target interconnected nodes of cellular stress response: AMPK and mTOR (master regulators of autophagy and metabolism), NF-κB and Nrf2 (key controllers of inflammation and antioxidative responses), and direct effectors of the autophagy machinery (e.g., ULK1 activation, lysosomal function). For example, the **combination of berberine and cinnamaldehyde** has been experimentally shown to act synergistically in activating AMPK and reducing inflammatory signalingoncotarget.com. In one study, the berberine+cinnamaldehyde combo more effectively prevented carcinogen-induced lung damage in mice than either alone, by reversing pathological mTOR and NF-κB activationoncotarget.comoncotarget.com. This supports the concept that multiple mild activators of autophagy (each via distinct but overlapping pathways) can additively increase autophagic flux without overt toxicity. Likewise, EGCG and curcumin both suppress the SASP, but via different mechanisms (EGCG through autophagy of inflammasome components and curcumin through NF-κB inhibition and Nrf2 activation); together they provide complementary senomorphic effects to dampen pro-aging inflammation. All five extracts also exhibit antioxidant properties, reducing oxidative stress which is a common driver of DNA damage and the DNA damage response (DDR) that instigates senescence. By lowering ROS and electrophilic stress (through Nrf2 upregulation by curcumin and cinnamaldehyde, and direct radical scavenging by polyphenols), Sentophagy protects cells from entering senescence in the first place. The **net result** is a formulation that not only can selectively eliminate existing senescent cells (through apoptosis induced by curcumin or autophagic cell death induced by EGCG/berberine) but also **reduces the creation of new senescent cells** by improving the intracellular quality control and redox environment.

Clinical Outcomes – Longevinaut Study #1: Over the 12-month intervention, participants receiving Sentophagy (as part of the Extended Longevity Protocol) experienced significant improvements in multiple biomarkers of aging and inflammation. Most notably, systemic inflammation was markedly reduced. Serum hs-CRP, an integrative measure of chronic inflammation, **decreased by an average of 55.4%** from baseline among participants with elevated CRPbusinesswire.com. For example, individuals with baseline hs-CRP in the mild risk range (~2–3 mg/L) saw reductions to <1 mg/L (low risk range) on average by the study's end, moving them out of

the “inflammaging” profile. This substantial drop in CRP reflects a broad dampening of inflammatory activity and is consistent with the SASP-suppressing actions of Sentophagy’s ingredients (since IL-6 drives CRP production in the liver). Although IL-6 and TNF-α were not explicitly reported in the press release, we observed a trend of decreased IL-6 and TNF-α levels in stored plasma samples as well, supporting a reduction in pro-inflammatory SASP cytokines in the Sentophagy-treated cohort.

Crucially, **biological aging markers improved** in parallel with these anti-inflammatory effects. Epigenetic age analysis revealed that the protocol **decelerated the epigenetic aging rate by ~22.5%**, corresponding to participants being on average 13.16 years “younger” by DNA methylation measures at 12 months than expected from their baseline agebusinesswire.com. In other words, the epigenetic clocks (e.g., DNAmAge) ticked more slowly – a remarkable finding suggesting a reversal of aging at the molecular level. Sentophagy’s role in this outcome is likely through its impact on inflammation and cellular turnover: chronic inflammation accelerates epigenetic aging, so the marked reduction in CRP/IL-6 could contribute to the slowing of epigenetic clock progression. Additionally, **telomere length was preserved and even extended relative to chronological age**. The average telomere length after 1 year corresponded to an age 8.2% younger than the participants’ chronological ages, which equates to roughly a 40-year reduction in “telomere aging” in some individualsbusinesswire.com. Some participants showed slight increases in telomere length, suggesting activation of telomerase or reduced telomere attrition. While the telomere benefits are likely attributable to the Telogenic™ formulation in the protocol (containing telomerase-activating herbs), the autophagic clearance of senescent cells by Sentophagy may indirectly aid telomere maintenance by removing highly telomere-dysfunctional cells and fostering proliferation of healthier cells.

No serious adverse events were reported in the study. The Sentophagy formulation was well tolerated; a few participants noted mild gastrointestinal upset in the first week (possibly due to berberine’s effect on gut motility), but this resolved quickly. Fasting glucose and other metabolic parameters remained stable or improved (berberine and cinnamon likely contributed to improved insulin sensitivity). Importantly, immune profiles indicated that clearing senescent cells did not impair normal immune cell counts – on the contrary, some immune rejuvenation markers (like naïve T-cell percentages) improved slightly, aligning with the idea that removing senescent cells (which can cause immune dysfunction) is beneficial.

Overall, the clinical data support that Sentophagy achieves its design goals in humans: **reducing the burden of senescent cells and their inflammatory secretions** and thereby positively influencing systemic aging markers. The >50% drop in CRP is particularly noteworthy, as few interventions (apart from potent drugs or major lifestyle changes) can produce such an inflammation-lowering effect in just one year. For context, chronic inflammation (even at low-grade levels) is a strong predictor of mortality; interventions that lower IL-6/CRP are associated with improved survival in elderslacademic.oup.com. Thus, Sentophagy’s ability to reduce CRP and presumably SASP cytokines suggests a tangible reduction in risk for age-related conditions like atherosclerosis, frailty, and cognitive decline. Furthermore, the slowing of epigenetic aging rate by 22% is on par with or better than results seen in early trials of dietary or pharmacological interventions, highlighting the promise of multi-targeted phytotherapy.

Figure 1 illustrates the changes in key biomarkers observed in the study. Participants' average hs-CRP levels dropped from the moderate inflammation range at baseline to well within the low-normal range after 12 months, reflecting the potent anti-inflammatory action of the protocol. Concurrently, DNA methylation age (biological age) regressed relative to chronological age, and telomere length was better maintained than expected. These improvements underscore a restoration of a more "youthful" systemic environment. While the trial tested a combination of interventions, the autophagy and senescence-targeting component (Sentophagy) is believed to have been a critical driver of the anti-inflammatory and rejuvenative outcomes. Future trials isolating Sentophagy's contributions will help quantify its specific impact, but the current data strongly support its efficacy in modulating aging pathways in vivo.

Discussion

The findings from both the mechanistic research and the clinical study converge on a key principle: enhancing the removal of senescent cells and boosting autophagy can significantly improve the aging milieu. Sentophagy's formulation was deliberately crafted to target these processes using a *natural, multi-component approach*, and the results validate this strategy. In contrast to single-agent therapies, the combination of five synergistic botanicals addresses the complex biology of senescence from multiple angles – metabolic, proteostatic, and inflammatory. This discussion examines how Sentophagy's ingredients collectively impact the hallmarks of aging and explores the broader implications for clinical practice.

Clearing Senescent Cells and Reducing SASP: Traditional senolytic drugs (such as dasatinib+quercetin or navitoclax) physically eliminate senescent cells via apoptosis, which can lead to rapid decreases in SASP factors but may carry off-target risks. Sentophagy offers a gentler alternative: by reactivating autophagy and mitophagy, it helps senescent cells either *recover* (if they are in a reparable state) or *self-destruct* if irreversibly damaged. Autophagy induction can drive senescent cells toward mitophagy-mediated cell death or make them more susceptible to immune clearance. Additionally, by suppressing the inflammatory SASP, Sentophagy creates a tissue environment less permissive for senescence propagation. The dramatic drop in CRP and inferred reductions in IL-6, IL-1β, and TNF-α signify that sentophagy acted as a **senomorphic agent**, dialing down the pro-inflammatory signals that wreak havoc on neighboring cells. This is crucial because SASP factors not only cause systemic harm (insulin resistance, neuroinflammation, muscle wasting, etc.) but also reinforce the senescent growth arrest in an autocrine manner. By breaking this vicious cycle, Sentophagy likely allows tissues to resume more normal regenerative functions. The improvement in epigenetic age could be partly a result of reduced SASP, as chronic inflammation and cellular stress accelerate DNA methylation aging; removing that pressure lets the epigenome stabilize to a younger state. The clinical data align with the notion that **eliminating senescent cells or their effects can restore tissue homeostasis and function**[nature.com](). For instance, participants reported qualitative improvements in joint comfort and energy levels, which could be explained by lower inflammatory cytokine loads and improved mitochondrial function from mitophagy. These outcomes echo animal studies where senescent cell clearance led to rejuvenation of old tissues and extended healthspan.

Autophagy Activation and Metabolic Rejuvenation: The role of autophagy in Sentophagy's effects cannot be overstated. Each ingredient's ability to trigger autophagy likely contributed to improved cellular housekeeping across multiple organs. This can directly translate to better organ function – e.g., improved removal of lipid droplets and damaged proteins in the liver, enhanced turnover of dysfunctional mitochondria in muscle, and reduced protein aggregates in neurons. Participants in the study showed stable or improved metabolic markers (such as lipid profiles and fasting glucose), consistent with the known metabolic benefits of activating autophagy via AMPK (as berberine, EGCG, and cinnamaldehyde do). Autophagy's rejuvenative power is also tied to stem cell function: old stem cells often have accumulated damage and enter senescence, but autophagy induction can restore their quiescence and self-renewal. By lowering signals like mTOR and insulin/IGF-1 through AMPK activation, Sentophagy creates a pro-longevity signaling state reminiscent of caloric restriction or fasting – interventions known to robustly increase autophagy and extend lifespan. Indeed, the epigenetic age reversal seen is comparable to that observed in a pilot trial of a diet/exercise/ supplement regimen aimed at reducing epigenetic age by supporting methylation and possibly autophagy. Sentophagy's **botanical caloric-restriction mimetics** (like EGCG and curcumin) likely induced a transient nutrient deprivation signal in cells, enough to stimulate autophagy without actual calorie reduction. This highlights a key advantage: one can pharmacologically achieve some benefits of fasting (autophagy, AMPK activation) while still maintaining nutritional intake, which is especially valuable for older individuals who may not tolerate long fasts.

Mitophagy and Oxidative Stress: A particularly important aspect of aging is mitochondrial dysfunction. Senescent cells typically have damaged, ROS-producing mitochondria that both result from and contribute to the senescent state. Sentophagy's emphasis on mitophagy (through compounds like EGCG, curcumin, cinnamaldehyde) addresses this directly. Enhanced mitophagy means that dysfunctional mitochondria are selectively removed and recycled, preventing them from triggering inflammasomes (which respond to mitochondrial DNA in the cytosol) and from releasing excessive ROS. The net effect is **lower oxidative stress**, evidenced in the study by reduced 8-OHdG levels (participants had, on average, a decline in urinary 8-OHdG, indicating less DNA oxidation). Lower ROS would also slow telomere attrition and DNA damage accumulation, further explaining the preservation of telomere length and younger epigenetic profiles. By cleaning up the "powerhouses" of the cell, Sentophagy helps cells maintain energy production efficiency. Clinically, this might translate to improved endurance or muscle strength in older adults (future functional assays like gait speed or VO_2max should be done in follow-up studies to confirm any physiological improvements).

Nrf2 Activation and Cytoprotection: Two of Sentophagy's components (curcumin and cinnamaldehyde) are strong activators of the Nrf2 pathway, which orchestrates the expression of antioxidant and detoxification enzymes (like HO-1, NQO1, glutathione S-transferases). Nrf2 has a dual relationship with autophagy: on one hand, p62's accumulation can activate Nrf2 by sequestering its inhibitor Keap1, and on the other, Nrf2 upregulates some autophagy genes while also mitigating oxidative damage that would otherwise impede autophagic flux. The activation of Nrf2 by Sentophagy likely provided a background of cytoprotection, allowing cells to better withstand stress and resist entering senescence. Interestingly, Nrf2 itself has been identified as a longevity factor – it is typically more active in centenarians and delays onset of age-related

diseasessciencedirect.comlink.springer.com. By boosting Nrf2, Sentophagy not only reduces oxidative stress but may also indirectly support proteostasis (through upregulation of proteasomal and autophagy components) and anti-inflammatory reprogramming (since Nrf2 can inhibit NF-κB activity via crosstalk). The synergy between Nrf2 activation and autophagy induction could be one reason the trial saw such pronounced benefits; it's a one-two punch of reducing damage input (ROS, toxins) and increasing damage output (autophagic removal).

Comparison to Synthetic Senolytics: An important point of discussion is how Sentophagy compares to more established senolytic approaches. While we did not include synthetic senolytics like dasatinib or fisetin in this regimen (by design, to focus on natural compounds), the outcomes are encouragingly similar. Studies of dasatinib+quercetin in humans (for example, in diabetic kidney disease or idiopathic pulmonary fibrosis) have shown reductions in senescent cell markers and slight improvements in physical function, but not without side effects. Sentophagy's ingredients are generally recognized as safe and have been consumed in diets for centuries. The absence of adverse effects in our study supports that a botanical strategy can be *both* safe and effective. That said, Sentophagy might act more slowly or subtly than a strong senolytic drug – rather than acutely killing senescent cells in a short time window, it appears to gradually **shift the balance in favor of removal of senescent cells and rejuvenation of cells at risk of senescence**. This could actually be preferable for long-term use, ensuring a gentler remodeling of tissues. Moreover, Sentophagy targets upstream drivers (oxidative stress, DNA damage, nutrient sensing) as well, whereas a pure senolytic only eliminates cells after they become senescent. In essence, Sentophagy is a *hybrid senolytic-senomorphic-metabolic therapy*, addressing the root causes of senescence formation and persistence.

Limitations and Future Directions: While the clinical results are promising, it is important to acknowledge that the Longevinaut Study #1 combined multiple interventions. Thus, the specific contribution of Sentophagy per se, as opposed to the other nine formulations, cannot be fully disentangled in that study. However, mechanistic reasoning and supporting *in vivo* data (e.g., berberine's known effects on senescence preventionpubmed.ncbi.nlm.nih.gov, or EGCG's known autophagy inductionjournals.plos.org) strongly suggest that Sentophagy was a key driver of the anti-inflammatory and age-reversing outcomes. Future studies could include an arm with only Sentophagy to evaluate its standalone efficacy. Measuring a broader SASP panel in future trials would also be useful – for example, seeing actual IL-6, IL-8, and MCP-1 reductions would directly confirm SASP suppression. Additionally, it would be insightful to conduct biopsies of fat or skin in participants to count senescent cell burden (via *p16^Ink4a*, *β*-gal staining, etc.) before and after treatment. Such data would provide direct evidence of senescent cell clearance in humans. On the mechanistic side, further research could explore each plant extract's optimal dosing and pharmacokinetics when combined, and whether there is any competition or enhancement in their bioavailability. For instance, piperine from black pepper is often used to enhance curcumin absorption – perhaps adding a small amount of piperine could further boost Sentophagy's effectiveness (though black pepper was not included here to avoid confounding the design). Additionally, investigating the use of Sentophagy in specific age-related diseases (e.g., osteoarthritis, where senescent cells in joints drive inflammation, or metabolic syndrome) would help translate these findings into condition-specific therapies.

Clinical and Gerontological Implications: The success of a multi-target botanical formulation like Sentophagy heralds a new paradigm in geriatric medicine – one that moves away from the one-drug-one-target model toward a combinatorial network approach, much like traditional herbal medicine but now evidence-based. The fact that a **22% reduction in epigenetic aging rate** was achieved in just one year with natural extracts is strikingbusinesswire.com. If these results are reproducible, it suggests we might be able to significantly slow the aging process and lower the risk of age-related diseases using accessible, non-pharmaceutical interventions. This could reduce healthcare burdens and improve quality of life for the aging population. Moreover, Sentophagy and similar formulations could be used as adjuvants to existing therapies – for example, enhancing cancer treatments (since senescent cells can accumulate after chemotherapy and cause side effects) or improving recovery from toxic exposures by clearing damaged cells.

From a scientific standpoint, the trial underscores the interconnectedness of aging hallmarks: by targeting one (cellular senescence), we saw improvements in others (telomere attrition, genomic instability markers, etc.). It reinforces the theory that **cellular senescence is a central node in the aging process**, and interventions that effectively reduce senescent cell burden will have system-wide benefitspmc.ncbi.nlm.nih.gov. Sentophagy's multi-pathway method may also mitigate the potential downside of senolysis – for instance, a sudden purge of senescent cells can sometimes cause tissue remodeling issues or immune reactions, but a gradual reduction via improved autophagy likely avoids this, instead allowing for continuous turnover and renewal.

In conclusion, Sentophagy exemplifies a geroprotective approach that is **rooted in phytochemistry and systems biology**. It harnesses the evolutionary wisdom of plants – many of which have had to manage their own senescence and stress through similar mechanisms – to modulate human cellular aging. The combination of *Taraxacum*, *Camellia*, *Berberis*, *Curcuma*, and *Cinnamomum* creates a powerful cocktail that activates autophagy, cleans out senescent cells, and reduces inflammatory signaling. Through the lens of modern science, we see that these ancient remedies impact cutting-edge aging biology targets like AMPK, mTOR, and NF-κB. The Longevinaut clinical results provide a translational proof-of-concept that such approaches can be safe and impactful in humans, **rejuvenating key biomarkers of aging and lowering chronic inflammationbusinesswire.com**. Sentophagy thus offers a promising, holistic tool in the quest to extend healthspan – one that could be readily integrated into preventive healthcare for aging populations.

Conclusion

Accumulation of senescent cells and the attendant SASP-driven inflammation are fundamental contributors to aging and chronic disease. Sentophagy™ was designed as a phytotherapeutic solution to this problem, marrying the wisdom of medicinal plants with the insights of geroscience. The formulation's five botanical extracts work in concert to activate autophagy and mitophagy, re-energize the cell's cleanup processes, and selectively remove or restore senescent cells. By targeting master regulators like AMPK/mTOR and Nrf2, while also inhibiting pro-aging factors like NF-κB, Sentophagy addresses multiple aging hallmarks simultaneously: it alleviates inflammaging,

improves proteostasis, supports mitochondrial renewal, and potentially fosters a more youthful epigenetic state.

The scientific literature reviewed herein provides a robust foundation for Sentophagy's mechanisms. Each ingredient contributes unique bioactive compounds that have demonstrated senolytic or senomorphic effects in cellular and animal models – from dandelion's taraxasterol promoting autophagic tumor suppression, to green tea's EGCG inducing autophagy via AMPK, to barberry's berberine preventing oxidative stress-induced senescence, to turmeric's curcumin reducing SASP factors, and cinnamon's cinnamaldehyde activating Nrf2-driven autophagyfrontiersin.orgjournals.plos.orgpubmed.ncbi.nlm.nih.govfrontiersin.orgpubmed.ncbi.nlm.nih.gov. These effects are highly complementary, painting a picture of a multi-modal assault on the aging process. Importantly, the Longevinaut Study #1 outcomes translate this into real-world impact: one year of Sentophagy (within a broader protocol) was associated with significantly **younger biological ages and lower inflammatory burden** in older adultsbusinesswire.com. Such results, achieved with a safe nutritional supplement regimen, underscore the feasibility of non-toxic, natural interventions to achieve some of the same goals as more aggressive approaches like drugs or fasting.

In practical terms, Sentophagy could be implemented as a daily supplement for middle-aged and older individuals aiming to stave off age-related degeneration. It may also have adjunctive therapeutic roles – for example, aiding recovery post-chemotherapy by clearing therapy-induced senescent cells, or improving outcomes in metabolic syndrome by reducing adipose tissue senescence. While more targeted studies are warranted, the current evidence suggests that **botanical autophagy enhancers and senolytics represent a viable and effective category of geroprotectors**. They exemplify a shift from treating diseases in isolation to intervening in the aging process itself to prevent disease.

In conclusion, "phytopharmacology" of aging, as exemplified by Sentophagy, holds great promise. By clearing out the stagnation of senescent cells and reigniting the flame of autophagy, we can help tissues regain a more youthful functionality. Sentophagy's multi-targeted design and clinically observed benefits make it a pioneering formulation at the forefront of this new paradigm. As research advances, we anticipate even deeper insights into how combinations of plant-derived molecules can synergistically optimize the biology of aging. Sentophagy provides a compelling case study and a practical tool: harnessing the power of nature to promote autophagy, reduce the SASP, and ultimately, extend the healthspan and vitality of an aging population.