UNIVERSITY OF BARCELONA

FACULTY OF PHARMACY AND FOOD SCIENCE

ANTI-AGEING SUPPLEMENTS
SCIENCE OR MARKETING?

Final Bachelor Thesis

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ABSTRACT

Ageing is known to be a multifactorial process that is driven by molecular changes, oxidative stress, inflammation, mitochondrial dysfunction and cellular senescence. In the last decades, the interest in strategies that promote healthy ageing has increased exponentially. This project reviews the scientific evidence of natural supplements with anti-ageing potential. Some of them are quercetin, resveratrol, curcumin, coenzyme Q10, collagen and NAD+ that have been related to improving metabolism, reducing inflammation, and supporting mitochondrial function, among others. Moreover, the project includes a contextualization and brief explanation about ageing mechanisms, besides the explanation of some groups of components with potential anti-ageing effects. The evaluation of the evidence suggests promising anti-ageing molecules, while the research still has some limitations in terms of population, size and doses used. Prospective larger and with clearer methodologies studies are still needed to confirm their benefits.

KEYWORDS

Ageing, senescence, anti-ageing, quercetin, resveratrol, curcumin, coenzyme Q10, collagen, NAD+, inflammation, antioxidant.

RESUM

Es coneix que l'envelliment és un procés multifactorial impulsat per canvis moleculars, estrès oxidatiu, inflamació, disfunció mitocondrial i senescència cel·lular. En les últimes dècades, l'interès per les estratègies que promouen un envelliment saludable ha augmentat exponencialment. Aquest projecte revisa l'evidència científica dels suplements naturals amb potencial antienvelliment. Alguns d'ells són la quercetina, el resveratrol, la curcumina, el coenzim Q10, el col·lagen i el NAD+ que s'han relacionat amb la millora del metabolisme, la reducció de la inflamació i el suport a la funció mitocondrial, entre d'altres. A més, el projecte inclou una contextualització i una breu explicació sobre els mecanismes de l'envelliment, a més de l'explicació d'alguns grups de components amb possibles efectes antienvelliment. L'avaluació de l'evidència suggereix molècules antienvelliment prometedores, tot i que la recerca encara té algunes limitacions pel que fa a la població, la mida i les dosis utilitzades. Encara calen estudis prospectius més grans i amb metodologies més clares per confirmar els seus beneficis.

PARAULES CLAU

Envelliment, senescència, anti-envelliment, quercetina, resveratrol, curcumina, coenzim Q10, col·lagen, NAD+, inflamació, antioxidant.

SDG

The final bachelor project has been aligned with the Sustainable Development Goals (SDG) 3, 10 and 17. For **SDG 3**, Good health and well-being, the reason is that the project has analysed the scientific evidence to prevent ageing and chronic pathologies coming from it, and in that way, contributes to the goal. The second, **SDG 10** (Reduced inequalities), also aligns with the project because it can inform the population about ageing inequalities, which can be exacerbated for this reason. The last, **SDG 17**

(Partnerships for the goals) focuses on the importance of the collaboration between different organisations such as academic institutions, professionals from different areas of expertise, companies and even countries for the promotion of healthy ageing.

INTRODUCTION

In recent years, there has been an increasing interest in the "anti-ageing" supplements. The longer senescence of the population, moreover, to the increase in health and wellbeing has promoted the research for solutions for a healthy longevity. In this context, dietary supplementation has gained a leading position as a tool to delay ageing signs and prevent pathologies associated with age, such as cardiovascular, neurodegenerative or metabolic diseases. (*EIT Food Healthy Ageing Think & Do Tank - EIT Food*, 2025)

Ageing is expected to be an important social problem worldwide in the upcoming decades. (*Ageing and Health*, 2025) The deterioration and functional decline of the body tissues or organs of older people caused by ageing increases the chances of age-related diseases, and that way, decreases the healthy life interval, which brings more pressure to countries all over the world in pension, medical expenses and health care aspects. For this reason, seeking effective therapies and understanding the biological mechanisms involved behind, may be a key point for such countries. (*EIT Food Healthy Ageing Think & Do Tank - EIT Food*, 2025)

However, its popularity, security and effectiveness are still debated in the scientific community. Some of the products are sold under promising conditions about the benefits they have for longevity, without solid evidence to support it. That way, it is crucial to analyse the existing literature to determine the real influence of those on the ageing process.

The last thing to consider is the key role of marketing behind those products. It often presents the products as an accessible and effective solution to combat the effects of ageing; however, sometimes, the background behind those is way too small to make such attributions.

All these contributed to defining the **objective** of this bachelor's project, which has been conducting a bibliographic review of the scientific literature published in the last 15 years, focusing on the biological mechanisms underlying ageing and the molecular pathways involved. Additionally, the project aims to describe and critically analyse the most relevant natural supplements that claim to have anti-ageing effects, with particular attention to their efficacy and mechanisms of action.

MATERIALS AND METHODS

The bibliographic research has been the main methodology for this project. Sources of information such as PubMed, Scopus, Elsevier, Nutrients and Molecules have been used as principal points for obtaining the references and results. They have been used to extract the information needed to guide the project. As the field is constantly growing and developing, the information has been restricted to the last 15 years, ensuring that the most accurate and up-to-date data. Besides, the articles included are either in English or Spanish, focusing on high-quality ones. Moreover, different keywords have been used to drive the search. As an example, some words used have been: "senescence mechanism", "ageing", "polyphenols ageing", "senescence compounds", "anti-ageing molecules". It is important to note that some compounds have more research behind them than others. For example, when typing "resveratrol ageing" in PubMed, 1821 results were found, whereas for "naringenin ageing", only 86 results were found. So, the components used for the review were also chosen because of the extension of the literature already published.

RESULTS

1. The ageing concept and the mechanisms behind

1.1. The definition of ageing

Ageing, as defined by the World Health Organisation (WHO) (*Ageing and Health*, 2025), is a natural process that involves the progressive accumulation of molecular and cellular damage over time. These changes lead to a gradual decline in physical and mental capacities while increasing the risk of developing various diseases, ultimately leading to death. However, these changes are not linear and vary between individuals. Beyond the biological aspects, ageing also includes important life transitions such as retirement, changes in housing and loss of loved ones.

Currently, societies worldwide face challenges in adapting their health systems and social assistance to this demographic shift. Population ageing is happening at a faster rate than in the past. In 2020, people aged 60 or older surpassed children under the age of five.

It is predicted that between 2015 and 2050, the percentage of inhabitants older than 60 will be nearly double, going from 12% to 22%. Additionally, it is also expected that by 2050, 80% of the elderly will be living in low- and middle-income countries. (*Ageing and Health*, 2025)

1.2. Molecular mechanisms behind ageing

The mechanisms behind ageing are complex and they include different important paths which have been studied and classified under nine "hallmarks of ageing". Those include genomic instability, shortening of telomeres, epigenetic alterations, loss of proteostasis, dysregulation in nutrient detection, mitochondrial dysfunction, cellular senescence, stem cell exhaustion and alteration in the intercellular communication. In this section of the manuscript, the most important paths and processes will be briefly explained. (López-Otín et al., 2013)

1.2.1. Genomic instability as a hallmark of ageing

The main effect of deoxyribonucleic acid (DNA) damage is genomic instability, which may produce changes in epigenetics, protein stress, impaired mitochondrial function, and dysfunction of the telomeres. This damage accumulates in the cells, potentially leading to cell death or senescence, as well as chronic inflammation, loss of function, atrophy and diseases in cells and tissues. (López-Otín et al., 2013)

Genomic instability produces permanent, transmissible DNA changes involving spontaneous deamination, hydrolysis, breaks and chemical modifications. DNA damage may result from abnormal structures or DNA processing intermediates, and it is a crucial factor in cancer and genetic diseases. However, the human body has repair systems that continuously act to preserve its integrity. Moreover, the shortening of the telomeres accelerates the ageing process, being also linked to DNA damage. (López-Otín et al., 2013; Li et al., 2024)

DNA damage causes alterations in chromatin, making it more prone to accumulate fragments related to the ageing of senescent cells. When this damage persists, it leaves epigenetic marks that generate variability between cells. Additionally, the transcription of senescent cells is more significantly altered than that of young cells. Because of that, the response to DNA damage could be a key factor in epigenetic changes that affect gene regulation, contributing to cellular heterogeneity and progressive deterioration of cellular function over time.

It is important to notice that despite all these negative effects, DNA damage may also have contributed to the evolution of species.

During ageing, some factors such as genotoxins, photo-ageing and mechanical stress continuously damage DNA. The majority of them are repaired; however, a small number escape the detection system, causing repair errors.

DNA damage is also associated with age-related diseases such as cardiovascular pathologies, Alzheimer and cancer. Moreover, defects in repairing proteins can cause premature ageing in different organs depending on the location of the alteration. In this context, the helicase RecQ has a key role in the stability of DNA, and its mutation is related to Werner, Bloom and Rothmund-Thomson syndrome. (Monnat, 2010)

On the other hand, the deficiency in nucleotide excision repair increases the risk of skin cancer and accelerates neurodegeneration. That way, failures in the repair mechanisms added to transcription can contribute to diseases such as osteoporosis, atherosclerosis and neurodegenerative disorders. Finally, DNA damage resulting from mitochondrial alterations is a key factor in several progressive diseases that affect different organs.

In summary, the defects in the DNA repair system contribute to the accumulation of genomic mutations, which lead to ageing in humans. This fact insinuates that there is a relationship between genome integrity and ageing. (Da Silva & Schumacher, 2021; Li et al., 2024)

1.2.2. Telomere shortening and dysfunction

Telomeres, structures at the ends of chromosomes, are composed of DNA and proteins, with the main function of protecting the genetic material and regulating the cell cycle. With each cell division, the telomeres gradually shorten, which limits the cells' ability to continue dividing. This shortening process is associated with cellular ageing and the development of various age-related diseases, given that the loss of telomere function affects both cell proliferation and survival.

The telomeres are conserved among the different organisms and they contain a repeated nucleotide sequence 3'-[TTA GGG]-5' in tandem, and going from few to multiple bases finishing at the 3′ end with a single chain of guanine-rich nucleotides of 75 to 300 constituting a "cap structure". (Li et al., 2024)

Shelterin complex is a special protein containing six units (TRF1, TRF2, TPP1, POT1, TIN2 and RAP1) that covers the telomeres. Its main function is to protect the chromosomes and regulate their length. (Li et al., 2024) Figure 1 schematizes the structure of telomerase and telomeres.

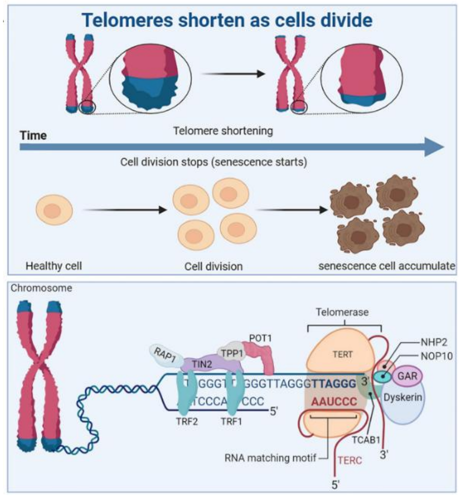

Figure 1: Structure of telomeres and telomerase and their relationship to senescence of cells. (Li et al., 2024)

The interaction between the shelterin complex and telomeres creates an optimal structure that contributes to maintaining genomic stability and therefore to DNA protection through mechanisms such as telomere capping, length regulation, and prevention of inappropriate DNA repair activities.

Consequently, the mutation in any of those six shelterin components (TRF1, TRF2, TPP1, POT1, TIN2, and RAP1) may compromise the integrity of this, potentially leading to telomere dysfunction and the onset of cell senescence.

With each somatic cell division, telomeres progressively shorten. Once they reach a critical length threshold, they can trigger cellular senescence and mitochondrial dysfunction, thereby contributing to the ageing of stem cells and the decline of tissue regenerative capacity. (Da Silva & Schumacher, 2021)

In this context, telomerase, which is a ribonucleoprotein, may be a key point when regulating ageing due to its ability to elongate and maintain telomeres. By counteracting telomere shortening, telomerase helps preserve chromosomal integrity and genomic stability. However, its activity presents two major challenges. First, telomerase is predominantly active in stem and progenitor cells, while its expression is nearly absent in most differentiated adult somatic cells. Second, its regulation, which is quite complex and context-dependent. At some point, the telomerase may be silent to prevent uncontrolled growth, while at another point it can be expressed to support tissue regeneration and cellular homeostasis. In addition, poorly understood factors including the tissue environment and epigenetic signals, may have a key role when regulating telomerase. All these make it a difficult target for therapeutic intervention. These regulatory complexities highlight the dual role of telomerase in both promoting longevity and preventing tumorigenesis, and underscore the challenges in developing safe and effective telomerase-based therapies. (Da Silva & Schumacher, 2021)

1.2.3. Mitochondrial and nutrient pathway dysregulation

An additional factor to consider in ageing is mitochondrial dysfunction. It includes different kinds of malfunctions, all affecting the mitochondria, such as dysregulation of proteins, alteration in the membranes, mitochondrial DNA (mtDNA) mutation and accumulation and disequilibrium in homeostasis of mitochondria. (López-Otín et al., 2013)

All these contribute to a decreased respiratory function, provoked mainly because of the increase in reactive oxygen species (ROS) production, electron leakage and reduction in adenosine triphosphate (ATP) generation. Therefore, cell function is directly dysregulated, causing senescence and stem cell exhaustion.

At the same time, energetic metabolism and pathways which detect nutrients are also affected by ageing. Some key pathways, such as insulin-like growth factor-1 (IGF-1), mechanistic target of Rapamycin (mTOR), AMP-activated protein kinase (AMPK) or sirtuins, are misadjusted, and that way is also the cellular response to the availability of nutrients. (Da Silva & Schumacher, 2021)

1.2.4. Cellular senescence, stem cell exhaustion and intercellular communication alteration

Cellular senescence is a response to cell stress or damage where the cell stops the permanent division process. Initially, this process is related to the protection against excessive proliferation of cells in cancerous processes; however, this progressive, exaggerated accumulation may lead to negative effects. Some substances which alter the tissue environment and contribute to the deterioration are produced by the senescent cells, for example, inflammatory molecules, enzymes and growth factors.

On the other hand, ageing not only decreases the number of stem cells but also reduces their functionality. That way, the tissue suffers a remarkable decline in its reconstruction capacity. Organs such as the skin, bowel or bone marrow are more affected because of their high cellular regeneration rates.

Lastly, the intercellular communication is also implicated. The main consequences are a decrease in immune function, increased low-grade chronic inflammation (*inflammaging*) and maladjustments in hormonal signalling. (Da Silva & Schumacher, 2021)

2. Strategies to delay ageing: diet, lifestyle, supplementation

Ageing is a multifactorial process that can be understood from two complementary perspectives: chronological ageing, which refers to the passage of time measured in years, and biological ageing, which reflects the functional and physiological decline of cells, tissues, and organs. While chronological ageing is inevitable and uniform, biological ageing varies significantly between individuals and can be influenced by genetic, environmental, and lifestyle factors.

After analysing the main paths behind ageing, the different lifestyle habits and therapeutic strategies to decelerate this process will be briefly exposed in this section. Biological ageing is influenced by a combination of genetic, environmental, and lifestyle factors. Among the most impactful strategies are: dietary patterns, caloric restriction, improving sleep quality, incorporating physical activity, nutritional supplementation or pharmacology with exogenous molecules targeting specific pathways. Figure 2 relates the different factors that can improve healthy ageing.

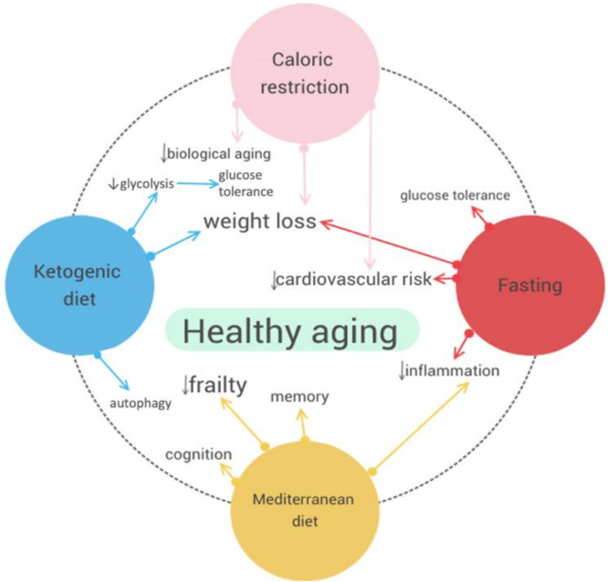

Figure 2: Interventions that help achieve healthy ageing. (Surugiu et al., 2024)

2.1.1. Diet and alimentary patterns

Currently, there is growing evidence of some dietary patterns and diets because of their protective effect for pathologies such as cardiovascular, neurodegenerative or metabolic. Some of these are Mediterranean, Japanese, vegetarian or ketogenic diets. (Mensah et al., 2025) Furthermore, many of these diets are naturally rich in antioxidants and polyphenols, such as flavonoids, resveratrol, and catechins, which contribute to cellular protection by neutralising ROS, modulating inflammatory pathways, and supporting mitochondrial function. These bioactive compounds are believed to play a key role in the anti-ageing effects of plant-based and traditional diets.

Mediterranean diet is known for the richness in vegetables, fruits, olive oil, fish, nuts and whole grain cereals, and the evidence relates it to less systemic inflammation, oxidative stress reduction and telomere length preservation. On the other hand, the Japanese diet, based on fish, soya, seaweeds and green tea, has been related to similar effects such as less inflammatory cytokines and better epigenetic regulation. (Mensah et al., 2025)

Likewise, moderate caloric restriction (but without malnutrition) has been remarked as one of the best interventions to decelerate ageing in animal models. It is believed to be mediated by key pathways related to metabolism, such as mTOR, AMPK and insulin signalling, which are related to longevity. (Surugiu et al., 2024)

Another pattern observed with interesting results is a low-protein and high-complex carbohydrate diet that may increase life expectancy in different organisms, probably because of the relation to autophagy, insulin sensitivity and oxidative damage reduction. (Mensah et al., 2025)

2.1.2. Lifestyle

Lifestyle has a strong correlation to the health status during the ageing process. Regular moderate physical activity contributes to a better mitochondrial function, a reduction in chronic inflammation and maintenance of muscular mass and osseous density.

Another key point is sleep quality, which allows the cells to repair, regulates hormonal secretion, for example, melatonin, which is involved in the sleep cycle, and it may increase the expression of protective genes. A clinical trial (Mochón-Benguigui et al., 2020) found higher concentration levels of "gene Klotho" in individuals who had better quality sleep. This gene is known for suppressing senescence and prolonging life when it is overexpressed.

Consequently, bad quality sleep has been related to higher risk of chronic inflammation, metabolic alterations and neurodegenerative pathologies. (Li et al., 2024; Mochón-Benguigui et al., 2020)

2.1.3. Nutritional supplementation and pharmacology

When we talk about supplementation, some studies suggest that some micronutrients may be antioxidant, anti-inflammatory or genic modulators and that way modulate ageing. Among the most studied there are resveratrol, vitamin E, vitamin D, selenium, folic acid and vegetal polyphenols. Those components have been associated with positive effects in genomic stability, telomere integrity and oxidative stress reduction. (Mensah et al., 2025) While it is not mentioned in any upcoming section, vitamin D has the potential to become the next anti-ageing molecule to focus on. For example, a recent study found that vitamin D3 supplementation significantly decreased leukocyte telomere length (LTL) attrition. (H. Zhu et al., 2025)

Moreover, some drugs such as metformin, sirolimus (rapamycin) or dasatinib have gained importance in the anti-ageing paradigm as they act within the hallmarks of ageing, for example, mTOR, mitochondrial or autophagy pathways, decreasing the age-related consequences. The clinical evidence is still not totally known, as it requires more evidence in humans. (Mensah et al., 2025; Kirkland & Tchkonia, 2020)

3. Pathologies related to ageing

The progressive accumulation of cellular damage and loss of functionality in different systems promotes the appearance of different chronic diseases. They not only share common risk factors such as oxidative stress, inflammation or mitochondrial dysfunction, but also are related to molecular mechanisms explained in the previous sections.

The first group of pathologies is the cardiovascular system ones. They are the main cause of mortality and morbidity in the older population. Endothelial dysfunction, increased oxidative stress, arterial rigidity, and low-grade inflammation (*inflammaging*) are processes closely related to vascular ageing. Moreover, the oxidised cholesterol accumulation in the arteries and the inflammasome NLRP3 activation make atherosclerosis more likely to happen, especially when the dietary patterns include high-saturated fats and refined sugars. (Mensah et al., 2025)

Another group to mention are neurodegenerative pathologies because of the alteration of brain homeostasis within older subjects. Some examples are the loss of synapses, misfolded protein accumulation (beta-amyloid or tau) and deterioration in mitochondrial and antioxidant functions. Thus, Alzheimer's or Parkinson's diseases may occur. Some diets, such as Mediterranean or Japanese, which include high anti-oxidative components like polyphenols, resveratrol or fucoxanthin, may have a protective effect. (Mensah et al., 2025)

Parallel to those, there are pathologies related to insulin homeostasis, which also are known to become worse with ageing. The main contributors are alterations in PI3K/AKT pathways, higher insulin resistance and more visceral fat accumulation. Therefore, those factors together with inadequate dietary habits contribute to the development of type 2 diabetes mellitus (T2DM) and metabolic syndrome. It has been observed that a vegetarian diet or caloric restriction may contribute to having better insulin sensitivity and reducing the risk of developing those pathologies. (Nunes et al., 2024)

Another factor associated is the loss of osseous mass because of ageing. This can develop into osteoporosis and therefore increases the risk of fractures. Within the pass of the years, there is a decrease in calcium and vitamin D absorption, an estrogenic deficit because of the postmenopausal state and systemic inflammation, which all contribute to osseous deterioration. Mediterranean diet, rich in calcium, magnesium, vitamin K and polyphenols, has been related to better osseous health and less risk of fractures in the elderly. (Mensah et al., 2025)

The last pathology to be mentioned in this section is sarcopenia, known as the progressive loss of mass and strength of muscle. This condition, which is highly related to ageing, increases the risk of falls, fractures and incapacity. The origin is multifactorial, including physical inactivity, anabolic resistance, chronic inflammation and a decrease of anabolic hormones. Diets that include an adequate protein balance and strength exercise are the most effective to prevent and handle it. (Mensah et al., 2025)

4. Bioactive compounds and supplements with anti-ageing potential

Before entering the upcoming section, some concepts will be clarified to understand the different paths in anti-ageing. (Gurău et al., 2018)

- **Senolytic:** Molecules with the ability to selectively eliminate senescent cells. Besides, they are related to ageing and chronic inflammation.
- **Anti-inflammatory agents**: Components that modulate the production and activity of pro-inflammatory cytokine levels and thus, reduce inflammatory response.
- **Senescence-associated secretory phenotype (SASP)**: A group of pro-inflammatory cytokines, chemokines, growth factors, and proteases released by senescent cells that contribute to chronic inflammation and tissue damage.
- **Sirtuins:** A family of nicotinamide adenine dinucleotide (NAD^+) dependent proteins involved in DNA repair, metabolic regulation, and cellular longevity. They

play a central role in maintaining genomic stability and are considered key regulators of the ageing process.

4.1. Bioactive compounds

4.1.1. Polyphenols

Polyphenols are a large bioactive compound group which are found in a wide variety of foods such as fruits, vegetables, pulses, tea, wine and cocoa. They are related to the ageing modulation because of processes such as mitochondrial dysfunction, oxidative stress, chronic inflammation and cellular senescence. (Gurău et al., 2018)

Polyphenols can be classified as flavonoids and non-flavonoids, including phenolic acids, stilbenes and lignans.

In Table 1, the most studied polyphenols are summarised, adding their main functions and classification into their main group.

Table 1: Classification of principal polyphenols with their action and dietary source. Own creation (Liu et al., 2024)

Polyphenol	Principal action	Dietary sources	Classification
Quercetin	Senolytic, anti-inflammatory, antioxidant	Onion, apple, broccoli	Flavonoid
Curcumin	Anti-inflammatory, SASP modulation, antioxidant	Turmeric	Polyphenol no flavonoid
Epigallocatechin Gallate (EGCG)	Antioxidant, anti-SASP, mitochondrial protector	Green tea	Flavonoid
Resveratrol	Sirtuins, antioxidant, mimics caloric restriction	Red grapes	Stilbene
Pterostilbene	Anti-inflammatory, epigenetic, neuroprotective	Blueberries	Stilbene
Genistein	Estrogen-like, epigenetic, antiinflamatory	Soy	Flavonoid
Naringenin	Antioxidant, senolytic, metabolic modulation	Citric fruits	Flavonoid
Kaempferol	Antioxidant, epigenetic, autophagy activation	Spinach, kale	Flavonoid
Apigenin	Flavonoid, anti-inflammatory, antitumoral	Parsley, chamomile	Flavonoid

4.1.1.1. Curcumin

Curcumin is the principal polyphenol, and it can be found in the *Curcuma longa* root. Traditionally, it has been used as a seasoning spice and a therapeutic agent in some groups of traditional families. The mechanism that involves the substance in the anti-ageing context is that it inhibits the nuclear factor-kB (NF-kB) pathway, which regulates the synthesis and expression of different inflammatory cytokines that have the SASP. Moreover, curcumin has an antioxidant function while it also acts as an epigenetic modulator because of the genes involved in oxidative stress and autophagy. (Nunes et al., 2024; Gurău et al., 2018)

4.1.1.2. Resveratrol

Resveratrol is one of the most studied anti-ageing polyphenols. It is included in the stilbene family. It is widely found in grapes, blueberries, wine and some nuts like peanuts. The function that has a potential anti-ageing effect is the activation of sirtuins (SIRT1), having an effect like caloric restriction. This way, it promotes the stability of genomics, autophagy and mitochondrial function. (Liu et al., 2024; Gurău et al., 2018)

4.1.1.3. Quercetin

Quercetin is a flavonoid that is widely found in fruits and vegetables like onion, apple or broccoli. Its main activity is the senolytic, which has been widely identified. In different ageing studies where quercetin is combined with dasatinib, the function has been demonstrated, and besides, it was found that it could reduce inflammation, decrease senescent cells and increase metabolic function of old people. (Liu et al., 2024)

Besides the senolytic effect, it also has an antioxidant and anti-inflammatory action because it inhibits the NF-kB and the expression of inflammatory cytokines of SASP. (Liu et al., 2024; Gurău et al., 2018)

4.2. Other bioactive components

Apart from polyphenols, there are also other bioactive components with potential anti-ageing effects. In Table 2, the most common components, their function and dietary sources are briefly explained.

Table 2: Resume of different bioactive components, principal action and diet sources. Own creation (Gurău et al., 2018)

Compound	Principal action	Dietary sources
Urolithin A (metabolite of ellagic acid)	Autophagy induction, enhances mitochondrial function, anti-inflammatory	Pomegranate, nuts
Ginsenosides	Antioxidant, anti-inflammatory, neuroprotection, decrease of senescent cells	Ginseng root
Spermidine	Autophagy induction, cognitive and cardiovascular protector	Curated cheese, soy, mushrooms
Oleacein	Anti-inflammatory, antioxidant	Extra virgin olive oil
Tocotrienols	Antioxidant, oxidative stress regulation and DNA damage	Palm and wheat bran oil, barley

4.3. Supplements and commercial formulations

4.3.1. NAD+

NAD+ is a coenzyme that mediates different pathways, the energy production, oxidative metabolism, DNA repair and epigenetic regulation. When talking about ageing, it has an important role because it is the cofactor for the enzymes of sirtuins and poly (ADP-ribose) polymerases (PARPs), which are related to cell survival, oxidative stress resistance and genomic stability. It has been observed that the levels of NAD+ decrease with the years, therefore contributing to mitochondrial dysfunction and cell damage.

The formulations available and used for the experimentation are mainly with precursors of NAD+, such as nicotinamide mononucleotide (NMN) and nicotinamide riboside (NR), because it is not possible to use NAD+ directly via oral administration. The reason is the low bioavailability associated. Those two molecules can help in restabilising intracellular levels of NAD+ and this way, decreasing ageing. (Li et al., 2024; M. Wang et al., 2024)

4.3.2. Coenzyme Q10

Coenzyme Q10 (CoQ10), also known as ubiquinone, is a lipophilic molecule that can be mainly found in cellular membranes and especially in mitochondria. The coenzyme contributes to the electron transport chain, which is indispensable for ATP production. Besides, it acts as an endogenous antioxidant because it protects lipids, proteins, and DNA from ROS.

Within ageing, the tissue levels of CoQ10 decrease progressively and especially in the tissues that have more energetic needs (muscle, brain and heart). These lower levels have been related to more mitochondrial dysfunction, oxidative stress and loss of cellular function. (Y. Wang et al., 2024)

4.3.3. Collagen

Collagen is a structural protein which can be found mainly in skin, muscles and articulations, specifically contained in connective tissue. After analysing the existing bibliography, it is mainly associated with skin ageing because it contributes to the maintenance of the extracellular dermic matrix. With the ageing process, the skin fibres of collagen are fragmented progressively, and there is a reduction in the new components. Apart from this, there is an increase in metalloproteins which reduce the collagen existing and that way decreasing the hydration, firmness, elasticity and wrinkle appearance of the skin.

The supplementation with collagen is always in the hydrolysed form, thus facilitating the absorption, bioavailability and stability of the molecule in the formulations because natural collagen is a complex and big molecule that would not have this capacity. (De Miranda et al., 2021)

Table 3 resumes and includes the supplements and commercial formulations from the previous section.

Table 3: Resume of the principal actions of NAD+, CoQ10 and collagen. Own creation.

Compound	Principal action
NAD+	Sirtuins activation, energetic improvement, mitochondrial support. (Li et al., 2024)
CoQ10	Mitochondrial support, cardiovascular improvement, lipid antioxidant. (Y. Wang et al., 2024)
Collagen	Structural support, skin improvement, muscles and articulations. (De Miranda et al., 2021)

Figure 3 schematizes the molecules and components mentioned in the sections above classifying them in the anti-ageing pathway where they are involved.

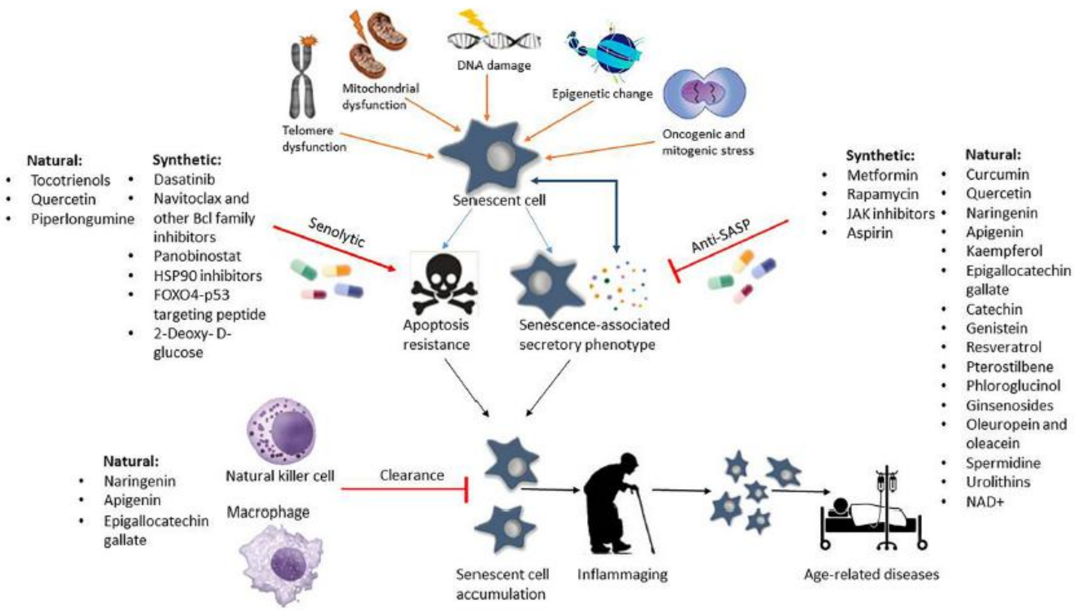

Figure 3: Components and their implication in the senescent cells pathway. (Gurău et al., 2018)

DISCUSSION

When the different studies that appear in Table 4 are analysed, it can be said that most of the components have not been studied for the anti-ageing effect *per se*, but have been used mainly in studies with pathologies in the context of age-related diseases or conditions where ageing is a contributing factor.

Quercetin has been used alone or in combination with other polyphenols, showing a potential reduction of oxidative stress markers and CD38. (Chong et al., 2024) It can also be combined with dasatinib, which has been related to senolytic effects in mice, improving inflammation, metabolism and mitochondrial function. (Liu et al., 2024) However, a major limitation of quercetin remains its low bioavailability, which varies depending on the formulation and delivery method.

Resveratrol seems to improve mitochondrial function and physical performance if it is combined with exercise in older adults who have functional limitations. (Harper et al., 2021) Another study showed anti-inflammatory effects in patients with T2DM. (P. Zhu et al., 2025) Despite these promising findings, the evidence is limited by small sample sizes, heterogeneity among studies, and variable methodological quality.

Curcumin demonstrated different anti-inflammatory and metabolic improvements, such as triglyceride, insulin resistance and inflammatory cytokines reduction. In some contexts like Alzheimer's disease (Thota et al., 2019) or fragility in older adults (Mankowski et al., 2023) curcumin has shown encouraging results. Nevertheless, further research is needed to confirm its efficacy and determine optimal dosing strategies.

Coenzyme Q10 showed improvements in endothelial and myocardial function, arterial elasticity, and hepatic steatosis in patients with MDASLD. (Vrentzos et al., 2024) This evidence is only for a specific population and needs to be further explored in different patients.

Collagen supplementation is strongly related to skin ageing benefits because of the improvement of hydration, elasticity and wrinkle reduction. (De Miranda et al., 2021) Additionally, it has shown potential in improving pain and joint function in patients with knee osteoarthritis (Simental-Mendía et al., 2024), suggesting broader applications beyond dermatological health.

Some NAD+ precursors, like NMN, have shown the ability to improve insulin sensitivity among other metabolic benefits. Besides, it has been related to reverse ageing-related gene expression patterns in mice. (Mills et al., 2016) Although human data remain limited.

Despite the promising findings, most of the studies lack evidence in the human population, while others apply to a specific population. Additionally, bioavailability and dosage remain critical factors influencing the efficacy of these compounds. For instance, lipophilic molecules such as resveratrol, CoQ10, and curcumin may require co-administration with high-quality dietary fats to enhance absorption—an aspect often overlooked in clinical trials.

Lastly, it should be considered the size of the studies, which was mostly not enough to draw such outcomes.

In conclusion, it is clear that most of the components have a path or a target which is clearly involved with ageing. However, the evidence demonstrates that there are still some gaps in the dosages, types of supplements or patients who suffer the anti-ageing benefits. That way, there is still a place for studies with a clear methodology that will probably lead to definitive conclusions about which are the most suitable components for each age-related pathology and in what dose. Such studies could pave the way for regulatory validation of specific supplements or drugs with anti-ageing claims, ultimately facilitating their integration into clinical practice and responsible marketing.

Table 4: Resume of the different studies included in the review. Own creation.

Component	Reference	Results	Limitations or considerations
Quercetin	(Chong et al., 2024)	The supplementation with quercetin combined with other polyphenols reduced CD38 and provided better levels of oxidative stress biomarkers.	• Short duration of the study • Small sample (n=30) • Low dose, similar to the one in the Mediterranean diet
	(Liu et al., 2024)	Combination of quercetin and Dasatinib improves inflammation, mitochondrial function and metabolism. The combination is also related to having senolytic effects.	• Evidence in mice • Limited bioavailability
Resveratrol	(Harper et al., 2021)	Resveratrol supplementation combined with exercise has better physical mitochondrial function.	• Only in old people with functional limitations, and combined with exercise. • Pilot randomised controlled trial
	(P. Zhu et al., 2025)	In T2DM patients, reduction of C-Reactive Protein (CRP), lipid peroxide (LPO), 8-isoprostanes levels, and oxidative stress scores (OSS). Increase of Glutathione peroxidase (GPx) and Catalase (Cat) levels.	• Size of the sample is limited • Low quality evidence (GRADE scale) • High heterogeneity
Curcumin	(Thota et al., 2019)	In Alzheimer's disease, curcumin supplementation reduced triglyceride levels, fasting insulin, insulin resistance and atherogenic index.	• The time of the intervention is limited • Only one dose of curcumin • Bioavailability is affected by lipids
	(Mankowski et al., 2023)	The supplement Curcumin C3 Complex ® had better performance in frailty measurements (knee extension, flexion peak) and lower levels of galectin-3 and IL-6.	• Bioavailability is affected by the specific supplement (Curcumin C3 Complex®)
CoQ10	(Vrentzos et al., 2024)	Improvement of endothelial and myocardial function, arterial elasticity and reduction of steatosis in patients with Metabolic Dysfunction Associated Steatotic Liver Disease (MDASLD).	• Controlled trial • Limited sample (n=60) • Only in the population affected by MDASLD
Collagen	(Simental-Mendía et al., 2024)	The meta-analysis suggests that patients with knee osteoarthritis (OA) could benefit from oral supplementation with collagen in terms of pain and function.	• Heterogeneous studies (dosage, collagen type and population) • Mostly knee OA • Limited duration
	(De Miranda et al., 2021)	In adults (50-year-old average), better skin hydration, elasticity and wrinkle reduction. The effects were visible after 4 weeks but more consistent after 90 days. The benefits remained visible after 30 days of suspending the supplementation.	• High heterogeneity in doses • Different sources of collagen (fish, pork, cow) • Mostly studied in women • Potential influence of other supplements
NAD+	(Mills et al., 2016)	Supplementation in mice with NMN (NAD precursor) improves metabolic parameters such as reduction of weight, better insulin sensitivity, lipid in plasma and reverses gene expression associated with ageing.	• Study in mice • Dose variability • Limited results to extrapolate to humans

REFERENCES

Ageing and health. (2025). Ageing and Health. https://www.who.int/news-room/fact-sheets/detail/ageing-and-health

Chong, J. R., De Lucia, C., Tovar-Rios, D. A., Castellanos-Perilla, N., Collins, C., Kvernberg, S. M., Ballard, C., Siow, R. C., & Aarsland, D. (2024). A Randomised, Double-Blind, Placebo-Controlled, Cross-Over Clinical Trial to Evaluate the Biological Effects and Safety of a Polyphenol Supplement on Healthy Ageing. *Antioxidants*, *13*(8), 995. https://doi.org/10.3390/antiox13080995

Da Silva, P. F. L., & Schumacher, B. (2021). Principles of the Molecular and Cellular Mechanisms of Aging. *Journal of Investigative Dermatology*, *141*(4), 951–960. https://doi.org/10.1016/j.jid.2020.11.018

De Miranda, R. B., Weimer, P., & Rossi, R. C. (2021). Effects of hydrolyzed collagen supplementation on skin aging: A systematic review and meta-analysis. *International Journal of Dermatology*, *60*(12), 1449–1461. https://doi.org/10.1111/ijd.15518

EIT Food Healthy Ageing Think & Do Tank—EIT Food. (2025). https://www.eitfood.eu/projects/eit-food-healthy-ageing-think-tank

Gurău, F., Baldoni, S., Prattichizzo, F., Espinosa, E., Amenta, F., Procopio, A. D., Albertini, M. C., Bonafè, M., & Olivieri, F. (2018). Anti-senescence compounds: A potential nutraceutical approach to healthy aging. *Ageing Research Reviews*, *46*, 14–31. https://doi.org/10.1016/j.arr.2018.05.001

Harper, S. A., Bassler, J. R., Peramsetty, S., Yang, Y., Roberts, L. M., Drummer, D., Mankowski, R. T., Leeuwenburgh, C., Ricart, K., Patel, R. P., Bamman, M. M., Anton, S. D., Jaeger, B. C., & Buford, T. W. (2021). Resveratrol and exercise combined to treat functional limitations in late life: A pilot randomized controlled trial. *Experimental Gerontology*, *143*, 111111. https://doi.org/10.1016/j.exger.2020.111111

Kirkland, J. L., & Tchkonia, T. (2020). Senolytic drugs: From discovery to translation. *Journal of Internal Medicine*, *288*(5), 518–536. https://doi.org/10.1111/joim.13141

Li, Y., Tian, X., Luo, J., Bao, T., Wang, S., & Wu, X. (2024). Molecular mechanisms of aging and anti-aging strategies. *Cell Communication and Signaling*, *22*(1), 285. https://doi.org/10.1186/s12964-024-01663-1

Liu, Y., Fang, M., Tu, X., Mo, X., Zhang, L., Yang, B., Wang, F., Kim, Y.-B., Huang, C., Chen, L., & Fan, S. (2024). Dietary Polyphenols as Anti-Aging Agents: Targeting the Hallmarks of Aging. *Nutrients*, *16*(19), 3305. https://doi.org/10.3390/nu16193305

López-Otín, C., Blasco, M. A., Partridge, L., Serrano, M., & Kroemer, G. (2013). The Hallmarks of Aging. *Cell*, *153*(6), 1194–1217. https://doi.org/10.1016/j.cell.2013.05.039

Mankowski, R. T., Sibille, K. T., Leeuwenburgh, C., Lin, Y., Hsu, F.-C., Qiu, P., Sandesara, B., & Anton, S. D. (2023). Effects of Curcumin C3 Complex® on Physical Function in Moderately Functioning Older Adults with Low-Grade Inflammation—A Pilot Trial. *The Journal of Frailty & Aging*, *12*(2), 143–149. https://doi.org/10.14283/jfa.2022.47

Mensah, E. O., Danyo, E. K., & Asase, R. V. (2025). Exploring the effect of different diet types on ageing and age-related diseases. *Nutrition*, *129*, 112596. https://doi.org/10.1016/j.nut.2024.112596

Mills, K. F., Yoshida, S., Stein, L. R., Grozio, A., Kubota, S., Sasaki, Y., Redpath, P., Migaud, M. E., Apte, R. S., Uchida, K., Yoshino, J., & Imai, S. (2016). Long-Term Administration of Nicotinamide Mononucleotide Mitigates Age-Associated Physiological Decline in Mice. *Cell Metabolism*, *24*(6), 795–806. https://doi.org/10.1016/j.cmet.2016.09.013

Mochón-Benguigui, S., Carneiro-Barrera, A., Castillo, M. J., & Amaro-Gahete, F. J. (2020). Is Sleep Associated with the S-Klotho Anti-Aging Protein in Sedentary Middle-Aged Adults? The FIT-AGEING Study. *Antioxidants*, *9*(8), 738. https://doi.org/10.3390/antiox9080738

Monnat, R. J. (2010). Human RECQ helicases: Roles in DNA metabolism, mutagenesis and cancer biology. *Seminars in Cancer Biology*, *20*(5), 329–339. https://doi.org/10.1016/j.semcancer.2010.10.002

Nunes, Y. C., Mendes, N. M., Pereira De Lima, E., Chehadi, A. C., Lamas, C. B., Haber, J. F. S., Dos Santos Bueno, M., Araújo, A. C., Catharin, V. C. S., Detregiachi, C. R. P., Laurindo, L. F., Tanaka, M., Barbalho, S. M., & Marin, M. J. S. (2024). Curcumin: A Golden Approach to Healthy Aging: A Systematic Review of the Evidence. *Nutrients*, *16*(16), 2721. https://doi.org/10.3390/nu16162721

Simental-Mendía, M., Ortega-Mata, D., Acosta-Olivo, C. A., Simental-Mendía, L. E., Peña-Martínez, V. M., & Vilchez-Cavazos, F. (2024). Effect of collagen supplementation on knee osteoarthritis: An updated systematic review and meta-analysis of randomised controlled trials. *Clinical and Experimental Rheumatology*. https://doi.org/10.55563/clinexprheumatol/kflfr5

Surugiu, R., Iancu, M. A., Vintilescu, Ștefănița B., Stepan, M. D., Burdusel, D., Genunche-Dumitrescu, A. V., Dogaru, C.-A., & Dumitra, G. G. (2024). Molecular Mechanisms of Healthy Aging: The Role of Caloric Restriction, Intermittent Fasting, Mediterranean Diet, and Ketogenic Diet—A Scoping Review. *Nutrients*, *16*(17), 2878. https://doi.org/10.3390/nu16172878

Thota, R. N., Acharya, S. H., & Garg, M. L. (2019). Curcumin and/or omega-3 polyunsaturated fatty acids supplementation reduces insulin resistance and blood lipids in individuals with high risk of type 2 diabetes: A randomised controlled trial. *Lipids in Health and Disease*, *18*, 31. https://doi.org/10.1186/s12944-019-0967-x

Vrentzos, E., Ikonomidis, I., Pavlidis, G., Katogiannis, K., Korakas, E., Kountouri, A., Pliouta, L., Michalopoulou, E., Pelekanou, E., Boumpas, D., & Lambadiari, V. (2024). Six-month supplementation with high dose coenzyme Q10 improves liver steatosis, endothelial, vascular and myocardial function in patients with metabolic-dysfunction associated steatotic liver disease: A randomized double-blind, placebo-controlled trial. *Cardiovascular Diabetology*, *23*(1), 245. https://doi.org/10.1186/s12933-024-02326-8

Wang, M., Cao, Y., Li, Y., Wang, L., Liu, Y., Deng, Z., Zhu, L., & Kang, H. (2024). Research advances in the function and anti-aging effects of nicotinamide mononucleotide. *Journal of Zhejiang University-SCIENCE B*, *25*(9), 723–735. https://doi.org/10.1631/jzus.B2300886

Wang, Y., Lilienfeldt, N., & Hekimi, S. (2024). Understanding coenzyme Q. *Physiological Reviews*, *104*(4), 1533–1610. https://doi.org/10.1152/physrev.00040.2023

Zhu, H., Manson, J. E., Cook, N. R., Bekele, B. B., Chen, L., Kane, K. J., Huang, Y., Li, W., Christen, W., Lee, I.-M., & Dong, Y. (2025). Vitamin D3 and marine ω-3 fatty acids supplementation and leukocyte telomere length: 4-year findings from the VITamin D and OmegA-3 TriaL (VITAL) randomized controlled trial. *The American Journal of Clinical Nutrition*, *0*(0). https://doi.org/10.1016/j.ajcnut.2025.05.003

Zhu, P., Jin, Y., Sun, J., & Zhou, X. (2025). The efficacy of resveratrol supplementation on inflammation and oxidative stress in type-2 diabetes mellitus patients: Randomized double-blind placebo meta-analysis. *Frontiers in Endocrinology*, *15*, 1463027. https://doi.org/10.3389/fendo.2024.1463027