



A Comprehensive Review on Ageing & Longevity

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ABSTRACT :-

Aging is a natural and intricate process characterized by gradual changes over time, which contribute to higher vulnerability to diseases and death. This article reviews various theories of aging, including programmed aging and damage accumulation hypotheses, and examines the genetic and environmental factors that shape aging. It discusses concepts like telomere shortening, hormonal imbalances, immune system changes, free radicals, wear and tear, somatic mutations, and the rate of living theory, providing a thorough understanding of how aging occurs.

The article also looks at ways to live longer, such as reducing calorie intake, exercising, using plant stem cell extracts, taking senolytic drugs, and gene therapy. These methods target the main causes of aging, improve cell health, and help people stay healthy for longer. They range from simple diet changes to advanced genetic treatments, providing different approaches to fighting aging.

Keywords: Aging, Longevity, Telomeres, senolytic drugs, programmed ageing, Damage accumulation, senescence.

INTRODUCTION:

Aging is a natural and complex process that has fascinated people for centuries. As we age, time affects our bodies, gradually reducing our physical and mental abilities. To understand aging better, many theories have been proposed. This review looks at different theories, starting with programmed aging, which includes ideas like telomere shortening, hormone changes, and immune system shifts, all of which explain how our bodies change over time. On the other hand, damage accumulation theories, such as the free radical theory, wear and tear theory, somatic mutation theory, rate of living theory, and cross-linking theory, provide reasons for the breakdowns and damage that occur as we age.

Beyond understanding the theories of aging, we also look at ways to slow down the effects of time. This part explores methods and treatments that show promise in reducing the aging process, giving hope for longer lives and better health.

Aging is a slow process where changes accumulate over time, making us more vulnerable to diseases and death. It happens in all living things and is influenced by both our genes and the environment. These factors affect how fast and in what ways we age. On a cellular level, aging happens when cells stop working properly and eventually die. This is influenced by both our genetic makeup and environmental factors. As we age, our body's ability to resist stress and maintain health declines, leading to frailty and death. The timing of this decline isn't clear, but it involves changes in the way our genes are activated and how our DNA is organized, which affects how well cells function and handle stress. When these processes go wrong, it plays a key role in aging. Studying these changes in our genes and DNA can help us understand aging better and may lead to ways to slow it down or even reverse it.

There are two main theories about why we age: programmed aging and damage accumulation. Programmed aging suggests that aging is a natural, predetermined process, while damage accumulation says aging happens because damage builds up in our cells over time. These ideas aren't completely separate, and both types of changes can happen in different species. The damage that occurs during aging can affect various parts of our cells and molecules.

Aging:-

Aging is a gradual process where changes accumulate over time, making individuals more vulnerable to diseases and death. This process occurs in all living organisms and is influenced by genetics, which explains the differences in lifespan between species and individuals. Environmental factors also play a role in how quickly and in what ways aging happens, which is connected to the makeup of our cells. Aging and death at the cellular level are controlled by genetics and environmental factors, with cell death occurring when important cellular functions deteriorate significantly.

As we age, the body's ability to maintain health and resist stress weakens, leading to frailty and eventually death. The exact timing of this decline is uncertain, but it involves changes in how genes are expressed and how DNA is structured, which affects cellular function and the ability to manage stress.

Disruptions in these processes are key to aging, and studying changes in the genome related to age could provide valuable insights into the aging process and possible treatments to delay or reverse aging and age-related diseases.

THEORIES OF AGEING:

There are two main ideas about why we age: programmed aging and damage accumulation. Programmed aging suggests that aging is a natural, built-in process, while damage accumulation argues that aging happens because damage gradually builds up in our cells and tissues. These ideas can work together, and different species may experience both. The damage that happens during aging can affect different parts of our cells and molecules.

1. PROGRAMMED AGEING:-

Programmed aging, or adaptive aging, is the idea that humans and other complex organisms have built-in biological processes that limit how long they live. These processes may have evolved because they provided some advantage in the past, even though they lead to aging and diseases like cancer or Alzheimer's today. This idea challenges Darwin's concept of "survival of the fittest," since aging doesn't help with survival or reproduction. While it was once dismissed, new research supports the theory, making it an important topic in the study of aging.

1.1 Telomeres shortening theory:

The telomere theory of aging says that cells age because telomeres—the protective caps at the ends of chromosomes—get shorter every time a cell divides. The subtelomere–telomere theory adds to this by highlighting the role of the DNA near the telomeres (subtelomeric DNA) in the aging process. Research shows that aging is connected to changes in genes, damage from stress, inflammation, and the way telomeres are protected. These processes lead to cells gradually aging and the body weakening over time.

This theory suggests that aging isn't just random wear and tear—it may be controlled by genetic systems and could potentially be altered. This challenges the belief that aging is purely a result of unavoidable damage over time.

1.2 Hormonal theory of ageing:

The Hormonal Stress Theory, or Neuroendocrine Theory of Aging, suggests that as we age, our body's ability to regulate hormones declines. This is mainly because the hypothalamus, which controls hormones, becomes less effective due to high levels of cortisol, a stress hormone. Unlike other hormones, cortisol levels stay high as we age, leading to problems like diabetes, thyroid issues, osteoporosis, and low blood pressure when standing.

Studies support this theory. For example, removing the pituitary gland (which controls hormones) in mice increased their lifespan, suggesting hormones play a role in aging. In some organisms, lower levels of a hormone called IGF-1 are linked to longer lives, though its effects on human aging are less clear.

Lifestyle changes like calorie restriction, exercise, and maintaining a healthy weight can improve hormonal balance, similar to what's seen in people who live over 100 years. However, using human growth hormone as an anti-aging treatment is not recommended.

1.3 The Immunological Theory:

As people get older, their immune system changes and becomes less effective. This makes seniors more vulnerable to infections like colds and the flu, as well as chronic inflammatory conditions like gout and arthritis.

The immunological theory of aging suggests that these changes in the immune system are not just a result of aging—they may actually cause many age-related problems and diseases. According to this theory, the immune system gradually weakens after its peak in puberty, leading to more infections, chronic illnesses, and contributing to the overall aging process and eventually mortality.

As we age, our immune system becomes less effective. Antibodies don't work as well, making it harder for the body to fight new diseases. This leads to stress on cells and can eventually result in death. Problems with the immune system have been linked to conditions like heart disease, inflammation, Alzheimer's, and cancer. However, it's not always clear if these immune changes directly cause these diseases.

2. DAMAGE ACCUMULATION THEORY:

Damage-based theories of aging suggest that aging happens because the body slowly accumulates damage to its systems over time, even starting before birth. This damage builds up and eventually causes organs or the whole body to fail. Some scientists believe aging is caused by different types of damage happening at the same time, meaning aging could be influenced by a mix of different processes.

2.1 Free radical theory:

As we age, damage builds up in our cells, especially in cells that don't divide. Mitochondria, which produce energy (ATP) for cells, are less able to repair DNA than the cell's nucleus. This leads to reduced energy production and more harmful molecules called reactive oxygen species (ROS). Damaged mitochondria release even more ROS, creating a cycle of damage that depletes energy and contributes to aging.

To protect against this damage, cells have antioxidants like enzymes (e.g., superoxide dismutase, catalase) and nutrients (e.g., Vitamin C and E). However, as we age, these defences become less effective, and ROS levels increase. This combination of more ROS and weaker defences is thought to play a major role in the aging process.

2.2 Wear and tear theory:

The wear and tear theory of aging, introduced by Dr. August Wiesmann in 1882, suggests that aging happens because cells and tissues slowly break down over time due to things like stress, radiation, toxins, and daily use. It compares aging to how machines, like cars, wear out with use. The theory is based on the idea that aging is an unavoidable result of physical and chemical laws.

However, this theory has been criticized. Scientists point out that our bodies have repair mechanisms and that organisms grow stronger during development rather than starting at their best. It also doesn't explain why similar species can have very different lifespans. Research has shown mixed support for this idea.

Some studies suggest that stress and illness speed up aging, while others show that mammals can handle stress without major problems. This means aging isn't just about wear and tear—it's influenced by many factors, including lifestyle, genetics, environment, stress, injuries, and diseases. Wear and tear might be part of the aging process, but it's more complicated than that.

2.3 Somatic mutation theory:

The somatic mutation theory of aging says that as we age, random mutations build up in the DNA of our body's cells (somatic cells). These mutations can turn off important genes, causing cells to work less effectively. Over time, this leads to organ failure, and when organs can no longer function properly, it can result in death.

This theory suggests that aging happens because of random damage to DNA, not because it's preprogrammed. Unlike mutations in reproductive cells (germ cells), which natural selection can filter out, mutations in body cells are harder for evolution to control, especially as they cause problems later in life. These mutations are thought to play a big role in aging and age-related diseases.

2.4 Rate of Living theory:

The rate of living theory of aging suggests that organisms age because they burn through energy quickly, especially when metabolizing oxygen. In the past, this idea was compared to how machines wear out with use. Today, scientists focus on how fast an organism uses oxygen to produce energy. Research shows that animals that process oxygen quickly, like small mammals with fast heartbeats, tend to live shorter lives. On the other hand, animals like tortoises, which have slower oxygen metabolism, tend to live much longer.

2.5 Cross linking theory of aging:

Crosslinking is a process where large molecules are bonded together, and it's been used in industry for a long time. It wasn't until the 1940s that scientists started to think it might be a key reason for age-related changes in the body. Crosslinking harms tissues by making them less elastic, reducing their ability to swell, increasing resistance to enzymes, and making them more brittle. There's evidence, both direct and indirect, showing that crosslinking is linked to aging. The body has various substances that cause crosslinking, including certain chemicals, free radicals, and metals. While some of these compounds work slowly, they can build up over time and contribute to aging.

As these crosslinking materials build up in the body, they create a stagnant metabolic pool. This makes age-related changes, caused by crosslinking, unavoidable over time.

3. LONGEVITY AND HOW TO ACHIEVE IT :

Throughout history, people have always sought ways to live longer and stay youthful. This desire has driven a lot of scientific research, leading to a wealth of knowledge on the topic. Scientists, researchers, and doctors have explored many different methods to fight aging, ranging from genetic treatments to lifestyle changes. These various approaches together form the foundation of efforts to slow down aging.

3.1 Healthy Diet:

Aging can be slowed down by taking preventive steps like eating foods rich in antioxidants, having a balanced diet, and taking care of your skin. Skin aging, in particular, is affected by oxidative stress caused by free radicals. Nutraceuticals—foods with health benefits—have gained attention for their ability to prevent and treat age-related diseases. These include functional foods, supplements, and herbal extracts that promote long-term health. Antioxidants in nutraceuticals, like carotenoids, flavonoids, and vitamins, help fight chronic conditions, especially diseases like Alzheimer's and cancer. They reduce inflammation, support the immune system, improve digestion, and enhance overall well-being.

3.2 Exercise:

As people age, they lose muscle strength and mass, a condition known as sarcopenia. This process starts around age 30, with muscle mass decreasing by about 0.3-0.5% per year. After 60, this decline speeds up, and by age 80, muscle mass can be reduced by half. Even short periods of bed rest, like during

a hospital stay, can cause a significant loss of muscle, especially in older adults, leading to weakness or difficulty moving. This loss of muscle increases the risk of falls and can lead to other problems, such as insulin resistance and issues with glucose metabolism. To prevent sarcopenia, it's important to regularly maintain muscle strength and mass.

Exercise can help in two main ways: strength training and aerobic exercise. Aerobic activities, like walking or biking, improve heart health and stamina.

3.3 Caloric restrictions:

Caloric restriction (CR) is a method that has been shown to increase lifespan and delay age-related diseases in lab animals. Early studies in the 1900s found that reducing the amount of food given to animals like rats slowed their growth and significantly increased their lifespan. This research made CR the main focus of anti-aging studies for most of the 20th century. It also showed that CR not only helps animals live longer but also reduces diseases and delays age-related problems.

Modern research has gone beyond CR to explore other ways to achieve similar benefits without reducing food intake. These include intermittent fasting, fasting-like diets, ketogenic diets, time-restricted eating, protein restriction, and limiting certain amino acids in the diet. While these methods share some effects with CR, they haven't always shown the same level of lifespan and health benefits.

3.4 Stem cells:

Plant stem cell extracts have anti-aging properties and can help fight the complex process of skin aging. Skin aging is influenced by both internal and external factors, with UV radiation being a major cause. UV rays create free radicals that damage the skin, leading to problems like collagen breakdown and the loss of the skin's protective barrier. Plant stem cells, which can be taken from various plants, have become popular in cosmetics because they can help repair the skin. These extracts contain active compounds that can extend the life of skin cells, improve skin elasticity, control cell division, and protect against UV damage.

A big reason plant stem cell extracts are effective is their antioxidant activity. They contain compounds like phenols and flavonoids that can neutralize free radicals, protect DNA from damage, and prevent harm to the skin's outer layer.

Kinetin, found in the stem cells of various plants, is an important compound that gives plant stem cell extracts their anti-aging benefits. It works as a powerful antioxidant, protecting proteins and DNA from damage caused by oxidation. Kinetin also helps produce enzymes that support regeneration and forms complexes with copper to activate self-repair processes in the body.

3.5 Senolytic drugs:

Senescent cells (SnCs) are cells that have stopped dividing but are still active. They become larger, show signs of DNA damage, and have changes in their structure. These cells also release harmful substances called the senescence-associated secretory phenotype (SASP), which causes inflammation and attracts immune cells to remove them. However, as we age, the immune system becomes less effective at removing these cells, causing them to build up. Even a small number of SnCs can cause chronic inflammation, damage tissues, and slow down the body's ability to repair itself.

These senescent cells are also found in many age-related diseases and play a role in causing them. Scientists are working on ways to identify and target these cells using markers and other techniques. Some studies suggest that eliminating these cells can help reduce age-related diseases and improve health. For example, drugs that target certain proteins in senescent cells can make them die, which has been shown to improve health in mice.

One combination treatment, involving dasatinib (a drug that blocks certain enzymes) and quercetin (a natural compound that affects cell pathways), has been shown to improve health and extend life in aged mice by improving heart function, endurance, and reducing frailty, bone loss, and other issues. Another compound, fisetin, has similar benefits, helping to reduce cell aging and damage in mice and even in humans. These findings show that targeting senescent cells could help improve aging and health.

3.6 Gene Therapy:

Gene therapy is becoming a promising way to treat age-related diseases. Originally used for genetic disorders that are inherited, gene therapy is now being tested for complex age-related conditions. It works by introducing new genes into the body, often using viruses or plasmids, to help reduce the effects of aging. These new genes can produce important molecules like growth factors or anti-inflammatory proteins that help fight aging.

Gene therapy can work in different ways, such as removing faulty genes, adding healthy genes to replace damaged ones, or editing genes to fix problems related to aging. Researchers are also exploring tools like antisense oligonucleotides and small RNA molecules to turn off genes that cause aging issues.

Advanced techniques like CRISPR and TALEN allow scientists to edit genes with great accuracy, targeting specific mutations that cause age-related diseases. In the future, gene therapy could play a key role in slowing down aging and treating age-related health problems.

CONCLUSION:

Aging is a complex process influenced by both our genes and environment. This review covered several theories about why we age, such as programmed aging, damage accumulation, and other factors like telomere shortening, hormone imbalances, immune system changes, free radicals, wear and tear, genetic mutations, and how fast we metabolize oxygen.

The review also discussed strategies for increasing longevity. These include eating a diet rich in antioxidants, exercising regularly to keep muscles strong and fit, reducing calorie intake to extend lifespan, using plant stem cell extracts for their anti-aging effects, taking senolytic drugs to remove old cells, and exploring gene therapy for treating aging-related diseases. These approaches range from lifestyle changes to advanced genetic treatments, offering ways to slow aging and improve quality of life as we get older. While aging is a natural process, ongoing research and new treatments bring hope for living longer, healthier lives.

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