A COMPREHENSIVE REVIEW ON ANTIAGING NATURAL PRODUCTS

A Project Report Submitted
In Partial Fulfillment of the Requirements
for the Degree of
BACHELOR OF PHARMACY

by

Abhishek Varshney
(Enrollment no.18021020135)

Under the Supervision of

Prof. Kalpana Pravin Rahate
Professor
Galgotias University
Greater Noida.

Department of Pharmacy
GALGOTIAS UNIVERSITY
Greater Noida
May, 2022

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GALGOTIAS UNIVERSITY

CERTIFICATE

This is to certify that project work entitled **"A COMPREHENSIVE REVIEW ON ANTIAGING NATURAL PRODUCTS"** done by **Mr. Abhishek Varshney** submitted to Department of Pharmacy, is a bonafide research work done under the supervision and guidance of **Prof. Kalpana Pravin Rahate ,** Professor, School of Medical and Allied Sciences, Greater Noida. The work is completed and ready for evaluation in partial fulfillment for the award of Bachelor of Pharmacy during the academic year 2021-2022. The project report has not formed the basis for the award of any Degree/Diploma/Fellowship or other similar title to any candidate of any University.

Date:

Prof. Pramod Kumar Sharma
Dean
School of Medical and Allied Sciences
Galgotias University
Greater Noida (U.P.)

BONAFIDE CERTIFICATE

This to certify that the project work entitled **"A COMPREHENSIVE REVIEW ON ANTIAGING NATURAL PRODUCTS"** is the bonafide research work done by Mr. Abhishek Varshney who carried out the research work under my supervision and guidance for the award of Bachelor of Pharmacy under Galgotias University, Greater Noida during the academic year 2021-2022. To the best of my knowledge the work reported herein is not submitted for award of any other degree or diploma of any other Institute or University.

Prof. Kalpana Pravin Rahate
Guide
Professor
School of Medical and Allied Sciences
Galgotias University
Greater Noida (U.P.)

DECLARATION

I hereby declare that the work embodied in this project report entitled **"A COMPREHENSIVE REVIEW ON ANTIAGING NATURAL PRODUCTS"** in Partial fulfillment of the requirements for the award of Bachelor of Pharmacy, is a record of original and independent research work done by me during the academic year 2021-22 under the supervision and guidance of **Prof. Kalpana Pravin Rahate** Professor, School of Medical and Allied Sciences, Galgotias University, Greater Noida. I have not submitted this project for award of any other degree or diploma of any other Institute or University.

Date: (Mr. Abhishek Varshney)
Place: **Name and Signature of candidate**

Acknowledgement

I would like to express my special thanks of gratitude to my project guide **PROF. KALPANA PRAVIN RAHATE** as well as our Dean **PROF. PRAMOD KUMAR SHARMA** who gave me the golden opportunity to do this wonderful project on the topic "**A COMPREHENSIVE REVIEW ON ANTIAGING NATURAL PRODUCTS**", which also helped me in doing a lot of research and I come to know about so many new things.
I new really thankful them.

Secondly I would also like a thank my friends who helped me a lot in finishing this project within the limited it helped me increase my knowledge and skills.
At last but not least , I would like to thanks GOD for gives me patience and power for the successful completion of the project.

ABHISHEK VARSHNEY

Abstract

Aging is typically characterised as the accumulation of a variety of harmful changes in cells and tissues as people become older, which are linked to an increased risk of disease and mortality. From the molecular to the organismic level, ageing changes are visible; environmental variables influence experimental findings; secondary effects confound the understanding of basic processes; and properly defined, readily measured "biomarkers" are missing. More than 300 ideas exist to explain the ageing process. Many of them are based on the analysis of cumulative changes over time. The free radical hypothesis of ageing, proposed originally by Harman and based on the molecular nature and ubiquitous existence of free radicals, is the most popular and thoroughly tested of all the hypotheses. Free radical reactions, according to the free radical hypothesis of ageing, induce ageing changes. According to the evidence, a healthy low-calorie diet combined with one or more free radical reaction inhibitors can extend average life expectancy at birth by 5 or more years. With growing age, the latter induces ageing changes at an exponentially rising pace. In developed countries, past advances in general living circumstances have reduced death rates to near-limit values; in these countries, the intrinsic ageing process is the leading cause of sickness and death beyond the age of 28. The average total number of years that a human anticipates to live is known as life expectancy. Life span, on the other hand, is the greatest number of years a human may live. While the average human life duration has stayed around 125 years throughout the past 100,000 years, life expectancy has grown noticeably (by 27 years in the previous century), particularly in Western countries. The eradication of most infectious illnesses that affect children and adolescents, improved cleanliness, and the use of medicines and vaccinations have all contributed to increased life expectancy.

1. INTRODUCTION

For all living species, ageing is an inescapable process. The ageing process begins at birth and becomes increasingly noticeable on the skin as we get older. In 2025, it is anticipated that there will be over 1.2 billion elderly individuals (over 60 years old) in the globe due to increased life expectancy.[1,2] Extrinsic variables such as sun exposure, smoking, nutrition, and pollution contribute to the ageing process, as do intrinsic factors such as genetics, cellular metabolism, hormone, and metabolic process. Aging is typically defined as the accumulation of a variety of detrimental alterations in cells and tissues as people become older, which are linked to an increased risk of disease and mortality. Aging is the result of a series of changes that occur as a person gets older, as well as the progressive changes that come with it. [3] Aging is the accumulation of changes that cause the sequential changes that come with becoming older, as well as the related gradual increases in the risk of illness and mortality. Disease, the environment, immunological malfunction, and an inborn process called ageing may all play a role in these alterations. As a result, with growing age, ageing changes at an apparently unchangeable and exponentially rising rate. Because of the exponential nature of the ageing process, the contribution of the ageing process to changes that occur with age is limited early in life but rapidly increases with age.[4] The average total number of years that a human anticipates to live is known as life expectancy. A human's life span, on the other hand, is the greatest number of years that he or she may live. While the average human life duration has stayed around 125 years throughout the past 100,000 years, life expectancy has grown noticeably (by 27 years in the previous century), particularly in Western countries. The eradication of most infectious illnesses that affect children and adolescents, improved cleanliness, and the use of medicines and vaccinations have all contributed to increased life expectancy.[5]

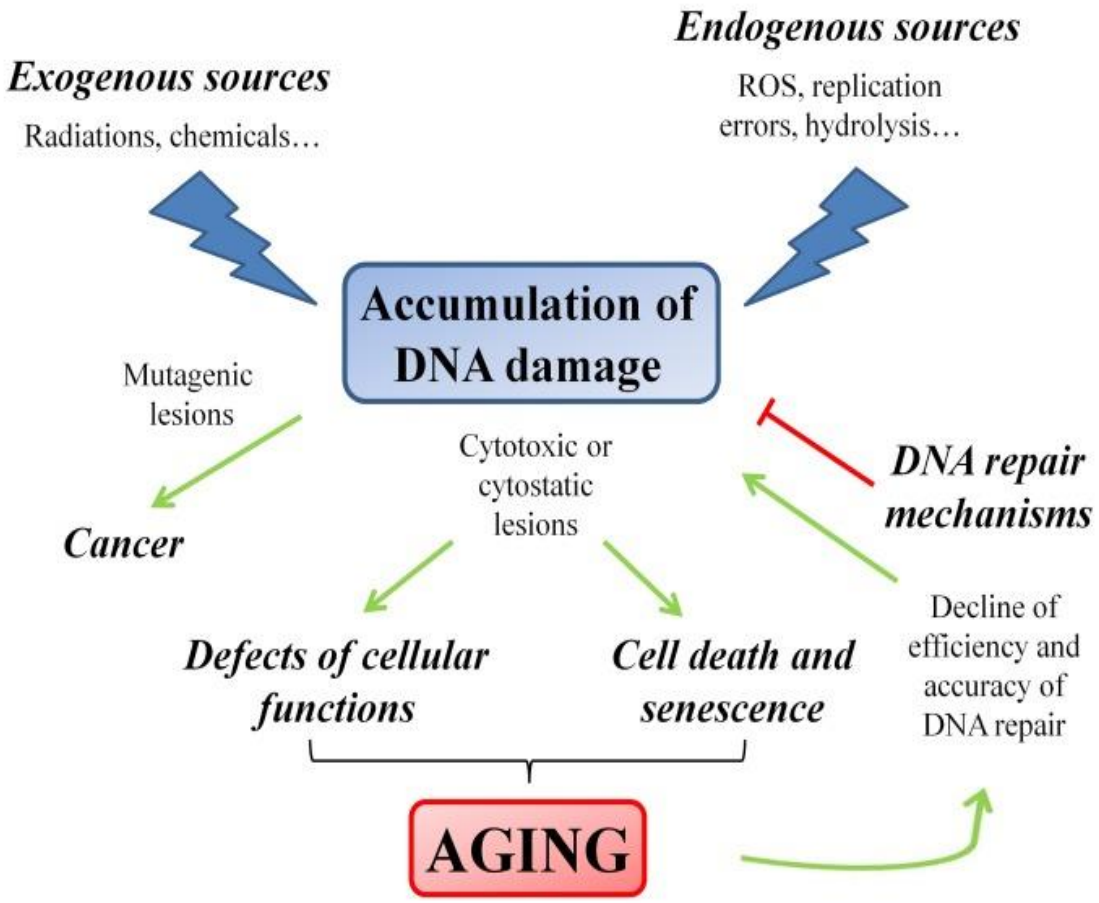


Figure 1 :- Representation of the pathway that modulate the aging process

2. THEORY OF AGING

To explain the ageing process, several ideas have been proposed. There is no universally recognised explanation: 'this observable process remains a mystery. it seems unlikely that a single hypothesis would explain all the causes of aging.[7] The primary theory of ageing is a formalisation of how natural selection may have influenced ageing.[8] In a work that constitutes the finest attempt yet to formalize the full evolutionary theory of ageing, Rose introduced the following theoretical concept of ageing: "A sustained fall in the age-specific components of fitness of an organism owing to internal physiological degradation is the proper definition of ageing to be employed here."[9,10]

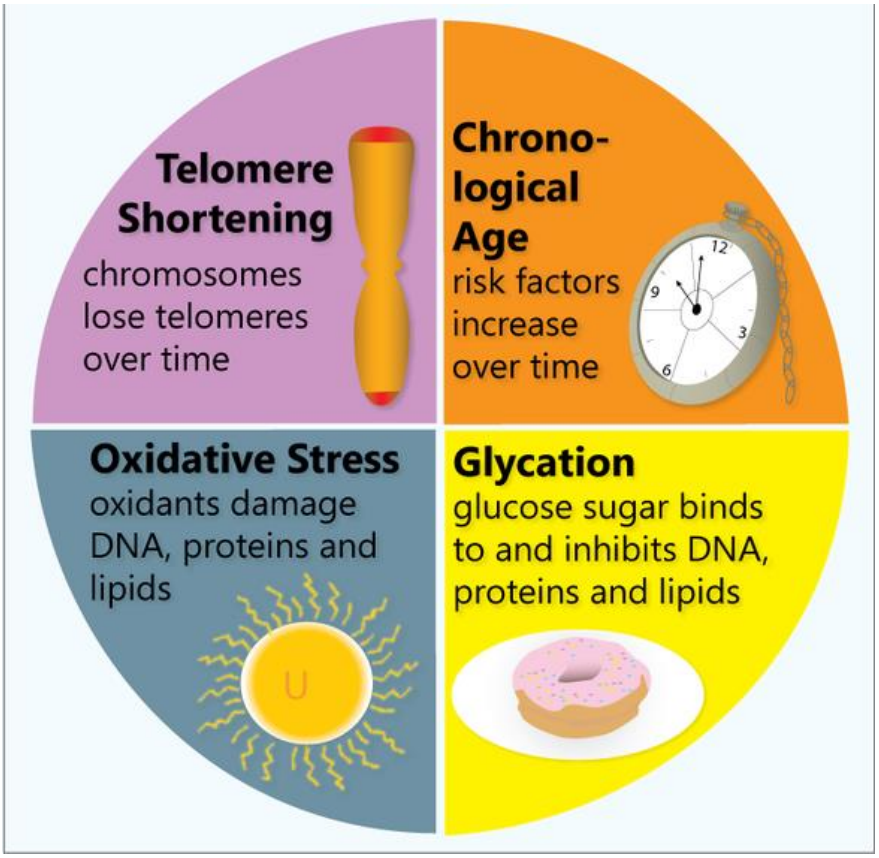


Figure 2 :- Some Factors In Aging

2.1. Characteristics of Aging

2.1.1. Mortality increases with age.

It posits, in particular, that the rate of individual disease in patients (aging) increases in early old age as the rate of damage healing slows. As a result, the rate of rise in mortality, which is thought to be linked to the rate of aging, increases.

2.1.2 Age-related changes in tissue biochemical composition.

The biochemical response to tissue injury is made up of local processes occurring within the region of damage and the systemic responses generated by the local injury via humoral and neuroendocrine pathways.

2.1.3. As people become older, their physiological capability decreases.

All organ systems have physiological changes as they age. Arteriosclerosis occurs when cardiac output declines, blood pressure rises, and arteriosclerosis develops. Gas exchange is impaired, vital capacity is reduced, and expiratory flow rates are slower.

2.1.4. As people get older, their capacity to adjust to external stimuli decreases.

Senescence is characterized by a decreased ability to maintain homeostasis.
Changes in relaxing or basal measures are less obvious than responses to external stimuli such as exercise or fasting..

2.1.5. Increased illness susceptibility and sensitivity.[6]

Many illnesses incidence and fatality rates rise with age, paralleling the exponential rise in mortality rates.

2.2. Evolutionary theory of aging

Aging is an aspect of the evolution of the entire life cycle, from conception to death, as studied in the branch of evolutionary biology known as life history evolution.[9] According to evolutionary theory, ageing is caused by a decrease in the force of natural selection. The observation of people with Huntington's disease, a dominant deadly mutation, led to the

development of this notion in the 1940s.[10] The influence of a variation in extrinsic death rates on intrinsic mortality rates (thus, longevity) as well as development, maturation, body size, and reproduction is predicted by evolutionary theory. When extrinsic mortality rates rise, the chances of surviving to a certain age decrease, and the power of selection declines quicker with age, resulting in an increase in intrinsic mortality. Evolutionary theories of ageing and longevity attempt to explain the striking discrepancies in known ageing rates and longevity records among biological species (compare, for example, mice and humans) through the interaction of mutation and selection mechanisms.[11,12] The desire to understand the biological evolution of ageing and longevity stems from perplexing observations of some biological organisms' life cycles. A bamboo plant, for example, may reproduce vegetatively (asexually) for up to 100 years, resulting in a thick stand of plants. The plants then all blossom at the same time, reproduce sexually, and die in the same season. The procedure is repeated about 100 years later (depending on the bamboo type).[13] This, as well as other comparable studies of "suicidal" living, is fascinating. This fascinating study, along with others of "suicidal" life cycles in species such as pacific salmon ,has fueled speculation that sexual reproduction may come at a penalty to species lifespan.[14] Thus, in addition to mutation and selection, the reproductive cost, or, more broadly, the trade-offs between distinct features of organisms, may play a role in the evolution of species longevity and ageing.[15] Because biological evolution is only conceivable for heritable manifestations of ageing, evolutionary theories of ageing are tightly linked to genetics of aging.[16]

2.3. Free radical theory of aging

The free radical theory of ageing developed in 1954 from a study of the ageing phenomena based on the hypothesis (Harman, 1992) that all living things age and die due to a single common mechanism that is controllable by genetic and environmental variables.[17,18] Free radical reactions occur today as a result of ionising radiation [19,20,21], nonenzymatic reactions such as those involving organic compounds [22,23,24], and enzymatic reactions, particularly those involving the two major energy-gaining processes used by living things: photosynthesis [25] and the reduction of 02 to water.[26,27,28] Because of the significance attached to delaying the ageing process, they are likely to develop in the reduction of terminal electron acceptors used by

anaerobes: most likely with NO3-, perhaps with CO2, and potentially with SO42-. in which 02 is the major source of harmful free radical reactions. The great majority of these free radical reactions are probably enzymatic in nature, involving maintenance and function, whereas the rest, using nonenzymatic mechanisms and 'leakage' of free radicals from enzymatic processes, result in more or less random changes.[29]

The free radical hypothesis of ageing offers plausible explanations for age-related phenomena like as

i. Among mammalian species, the link between average life lengths and basal metabolic rates,
ii. The occurrence of a cluster of degenerative illnesses in later life,
iii. The longevity-enhancing impact of dietary restriction,
iv. Females' greater longevity,
v. The age-related rise in autoimmune symptoms[30,31]

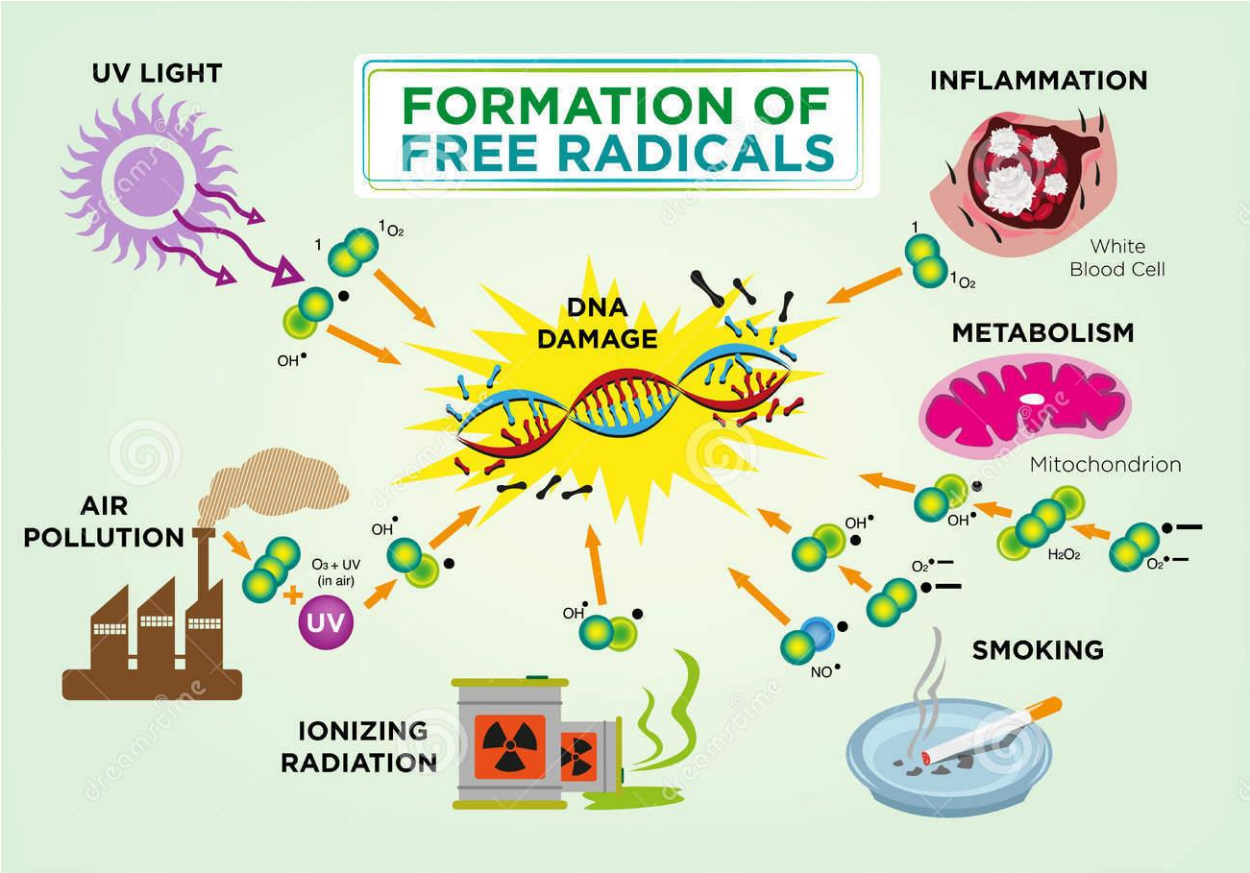


Figure 3 :- Formation of Free Radicals

2.4. Mitochondrial theory of aging

Harman proposed the initial version of the mitochondrial theory of ageing, which proposed that the ongoing accumulation of free radical damage to the mitochondria is the major driving force behind the ageing process.[32] Mitochondria are organelles that are found in nearly every eukaryotic cell. Mitochondria are now widely considered to be endosymbionts that evolved from purple bacteria 1.5 x 109 years ago.[33] Mitochondria are cellular energy factories that produce ATP by combining hydrocarbons and oxygen. There are hundreds of mitochondria in every human cell, and each mitochondrion contains multiple copies of mitochondrial DNA (mtDNA).[34] Mitochondria are cellular organelles that use oxygen to make energy (ATP). The UV action on the mitochondrial electron transport chain generates a lot of reactive oxygen species (ROS), which can damage mitochondrial DNA (mtDNA). The mitochondrial genome encodes 13 components of the electron transport chain, and oxidative damage can cause DNA

deletions or rearrangements, most likely due to double-strand breaks, which might impair mitochondrial energy production. It is hypothesised that the resulting reduction in mitochondrial activity in photodamaged skin leads to an increase in ROS production and further limits the cell's capacity to commence energy production.[35]

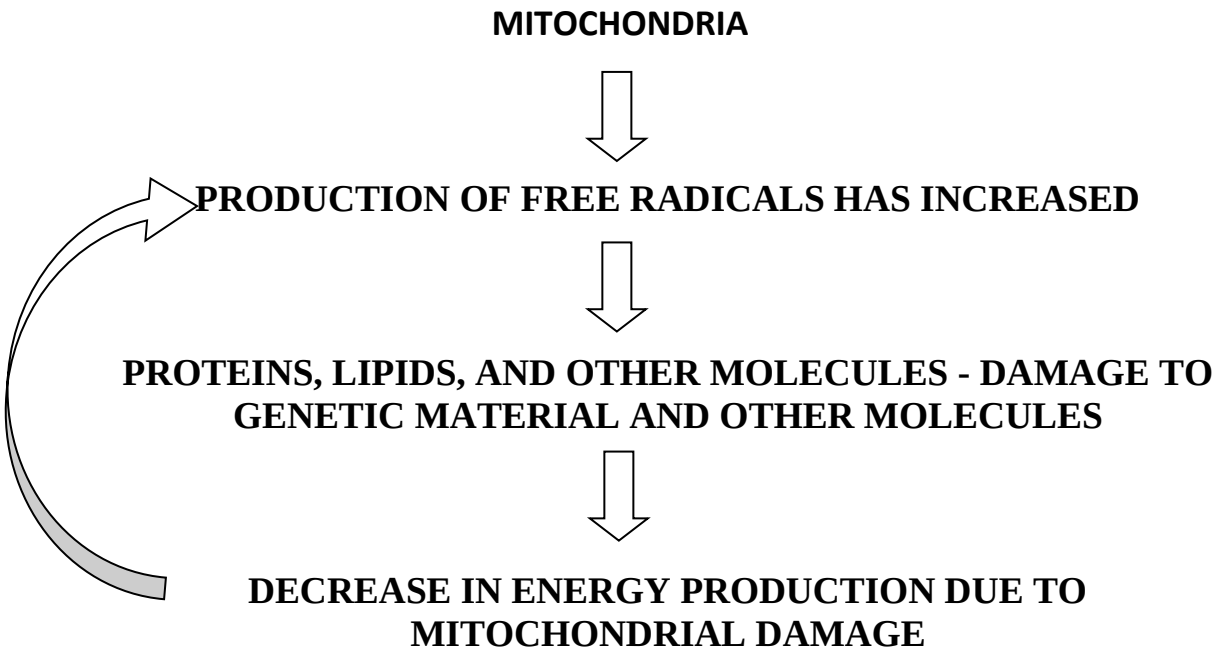
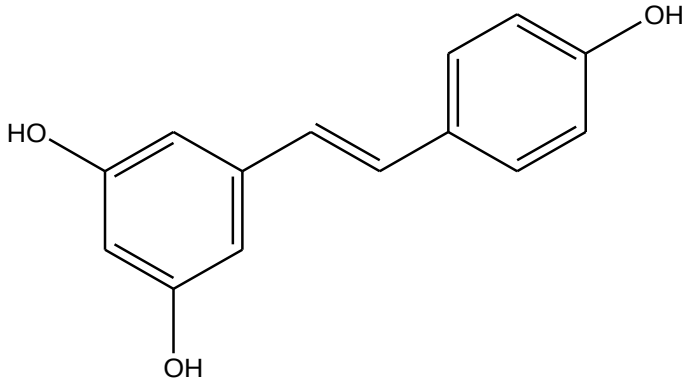
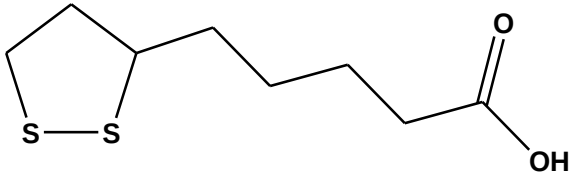


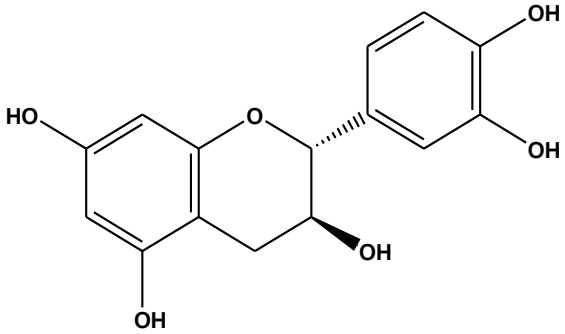
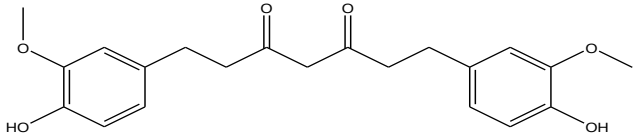
Figure 4 :- Process Mitochondria Damage

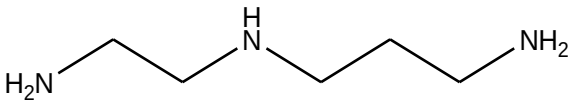
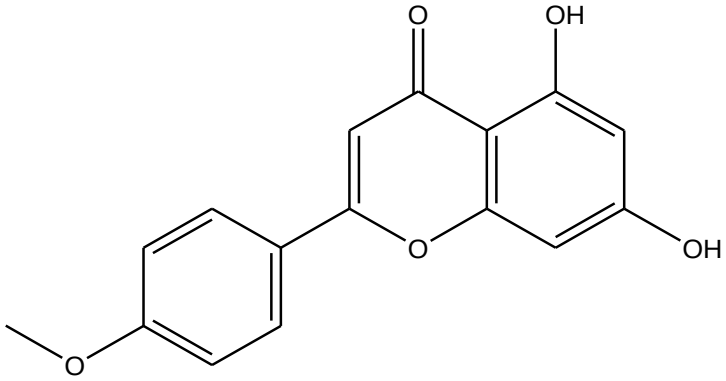
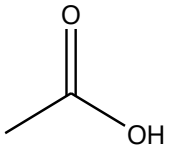
3. ANTI-AGING COMPOUNDS DERIVED FROM NATURAL SOURCES

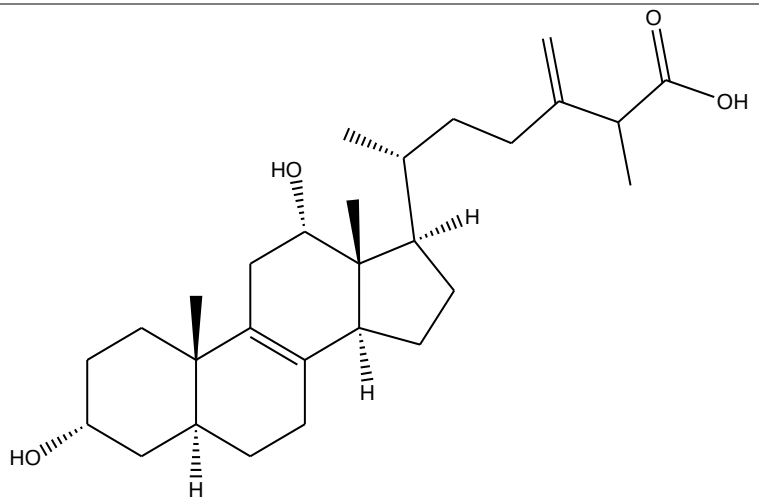
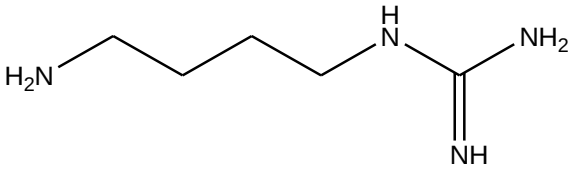
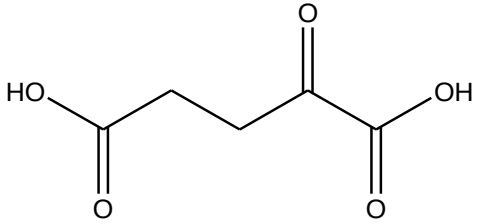
Since ancient times, anti-aging therapies have piqued people's attention. Anti-aging activities are designed to extend life and improve quality of life. Anti-aging activities are used to treat age-related ailments such Parkinson's disease (PD), Alzheimer's disease (AD), cardiovascular disease, cancer, and chronic obstructive pulmonary disease. Natural products are well-known for their ability to slow down the aging process by affecting metabolic pathways, resulting in a longer lifetime. These natural chemicals are being used in drug design and development for effective pro-longevity medications using computational and high throughput approaches. Natural compounds include a vast array of structural scaffolds that can be used to develop prospective candidate chemical entities for the important healthcare problem of extending life span and/or postponing aging. Natural substances (in either pure form or extract form) that have been discovered to postpone cellular senescence or in vivo ageing will be critically evaluated in this article. There are about 300 chemicals that have anti-aging properties. We've compiled a list of chemicals or natural product extracts having anti-aging properties. Furthermore, the chemical structures of the found natural compounds will be given and analyzed, along with the CAS No. [Chemical Abstracts Service Number], Source, Chemical Structure, Anti-aging action, and mechanism.

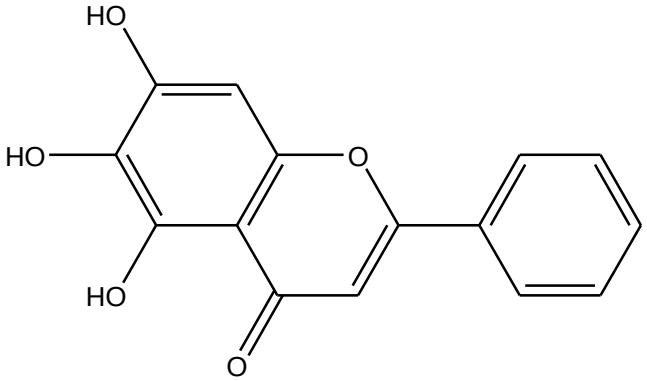
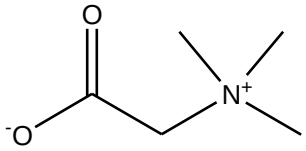
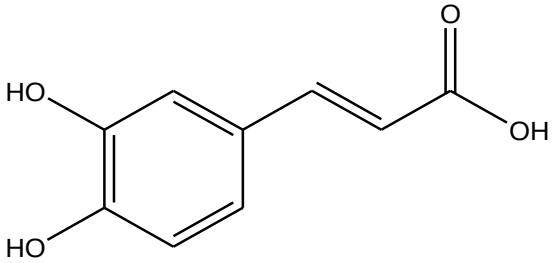
Table :- Anti-aging compounds derived from natural source

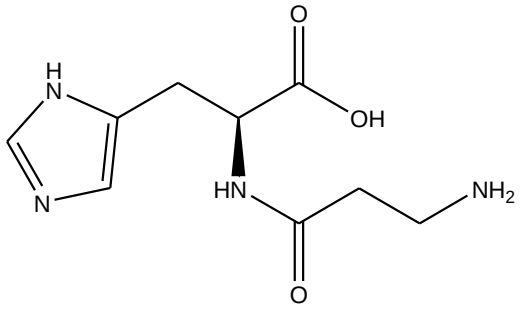
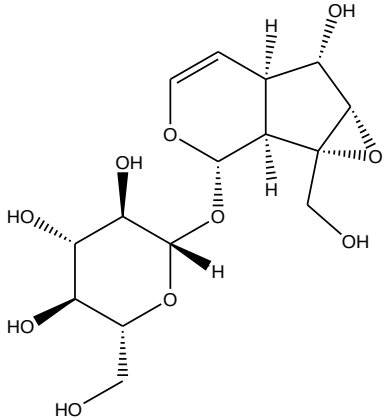
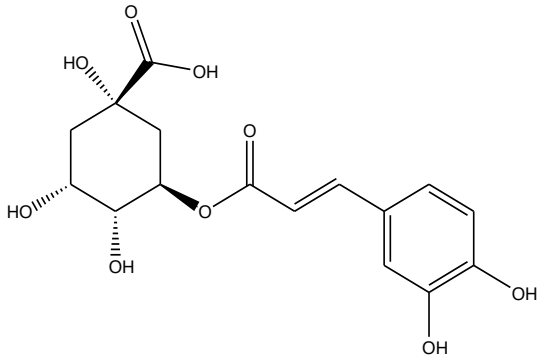
S. NO.	Chemicals Name And CAS NO.	Chemicals Structure	Source	Anti-aging activity and mechanism
1.	Resveratrol 501-36-0		Grapes	proteasomal degradation, AMPK, autophagy, and SIR-2.1 are all regulated, resulting in an 18.0% increase in average longevity. [36.37.38]. 70.0 percent increase in average lifetime; SIR2 and SNF1 regulation [39,40]
2.	Alpha-Lipoic acid 62-46-4		Broccoli, Beets, tomatoes	The average lifespan and antioxidant levels have increased by 12.0%.[41] Antioxidant, enhancing chemotaxis index. has increased by 24.0 percent.[42]

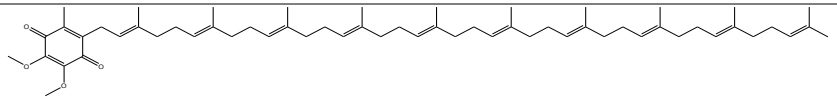
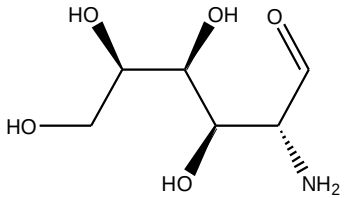
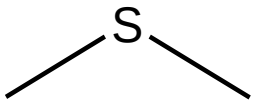
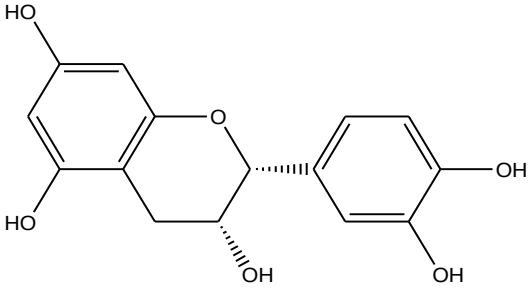
3.	Catechin 154-23-4		Apples, grapes, green tea, and cocoa	The average lifespan and antioxidant levels have increased by 16.0 percent. [43,44] DAF-2, AKT-2, MEV-1, and NHR-8 are all regulated, whereas insulin-like growth factor-1 is reduced, resulting in a 13 percentage increase in average longevity and antioxidant protection..[45]
4.	Curcumin 458-37-7		turmeric (Curcuma longa)	The average lifespan and antioxidant levels have increased by 25.8%.[46] The average lifetime and antioxidant levels have increased by 25.0 percent.[47]

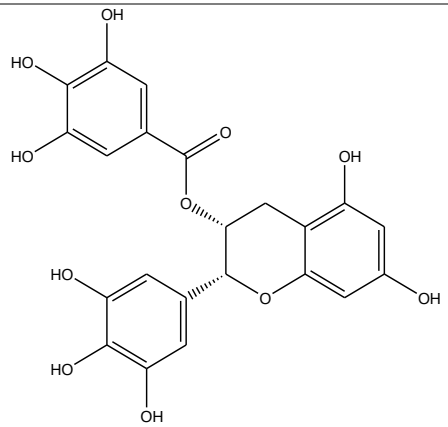
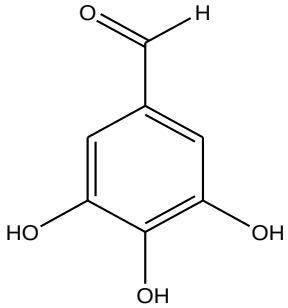
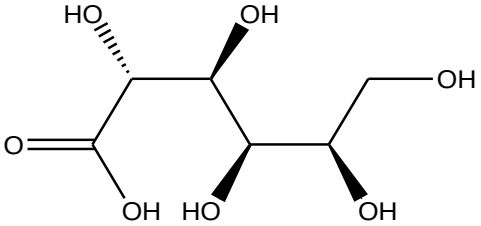
5.	Spermidine 124-20-9		aged cheese, mushrooms, soy products	Autophagy and mean life duration both increased by 30%. There was a 15.0 percent increase in average lifespan and autophagy.[48]
6.	Acacetin 480-44-4		safflower seeds	Upregulation of SOD-3 and GST-4 and a 27.3 percent increase in average lifetime.[49]
7.	Acetic acid 64-19-7		apples, grapes, oranges, pineapple	Regulation of the insulin/IGF-1 pathway resulted in a 23.0% increase in average longevity.[50]

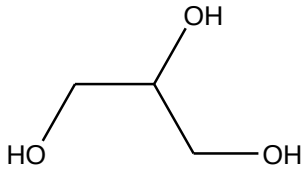
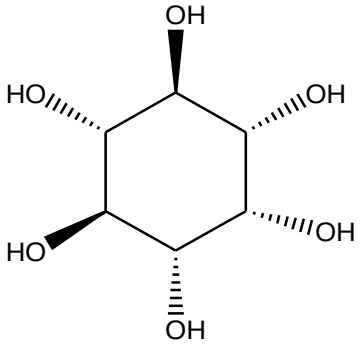
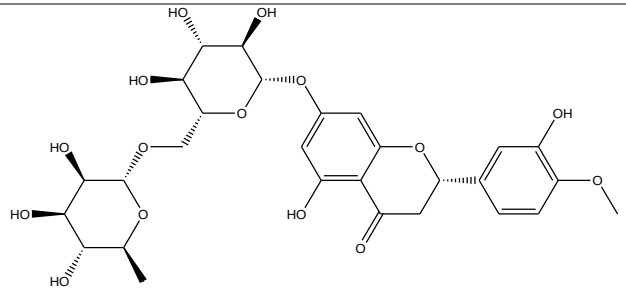
8.	Antcin M 1005344-44-4		Antrodia cinnamomic	Antioxidant, which regulates Nrf2 and SIRT-1, leads to a 10.0 percent increase in average lifetime. [51]
9.	Agmatine 306-60-5		Generatedby arginine decarboxylase	The average longevity has increased by 16.0%, indicating that more study is needed. [52]
10.	Alpha-Ketoglutarate 328-50-7		Tricarboxylic acid cycle intermediate	Inhibiting ATP synthase and TOR signalling resulted in a 50.0 percent increase in average lifetime. [53]

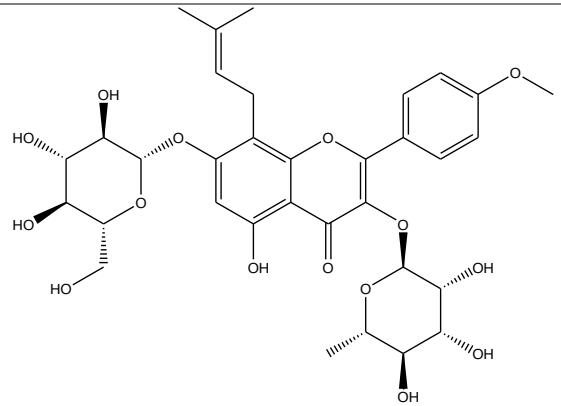
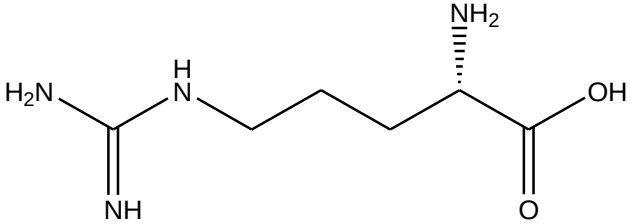
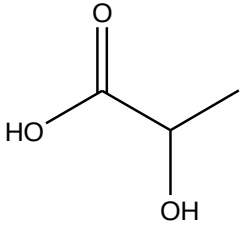
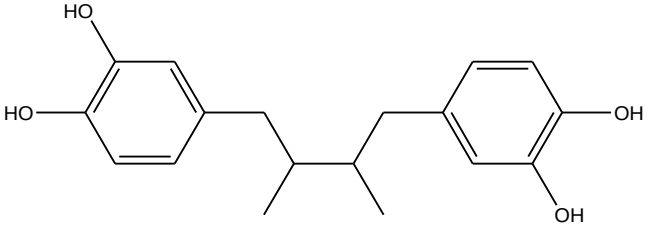
11.	Baicalein 491-67-8		Scutellaria baicalensis	The average lifespan and antioxidant, regulating SKN-1 increased by 24.0 percent.[54]
12.	Betaine 107-43-7		Beets, Spinach, Grains	The average lifetime has increased by 9.0 percent, indicating that further study is needed.[55]
13.	Caffeic acid 331-39-5		Apples, berries, pears	Increasing the average lifespan by 11.0 percent and controlling OSR-1, SEK-1, SIR-2.1, UNC-43, and DAF-16.56 are all OSR-1, SEK-1, SIR-2.1, UNC-43, and DAF-16.[56]

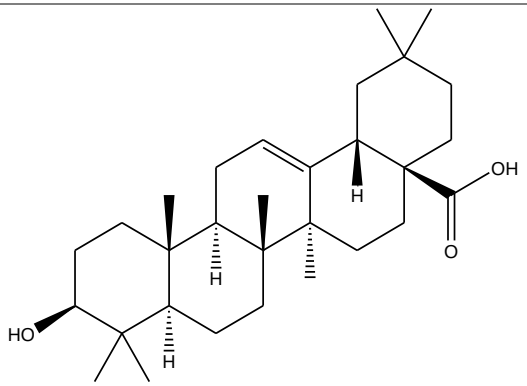
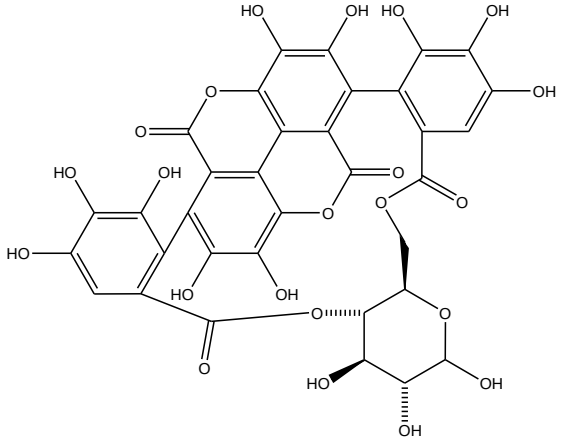
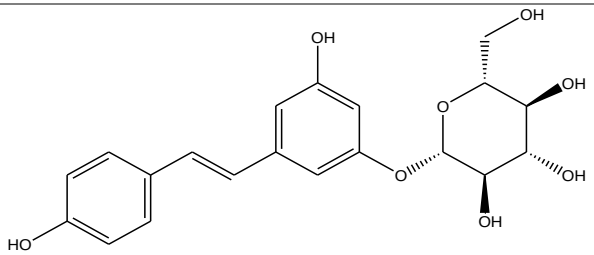
14.	Carnosine 305-84-0		Endogenous dipeptide	The average lifespan and antioxidant levels have increased by 26.0 percent. [56,57]
15.	Catalpol 2415-24-9		Rehmannia glutinosa	DAF-16 and SKN-1/Nrf regulate DAF-16 and SKN-1/Nr, resulting in a 28.5 percent increase in average longevity and antioxidant.[58]
16.	Chlorogenica cid 327-97-9		Coffee, tea	20.1 percent increase in average lifetime and antioxidant activity, indicating that the IIS pathway is being regulated.[59]

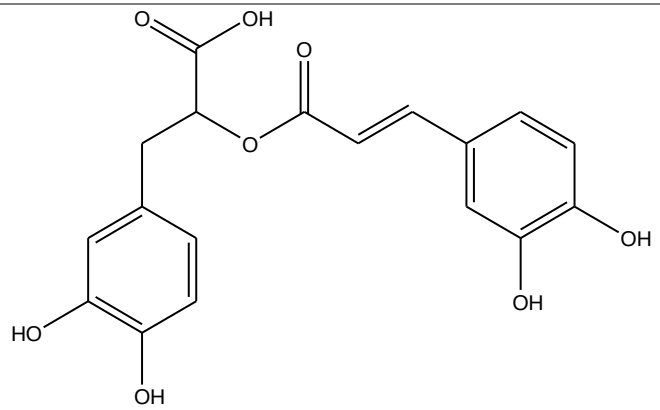
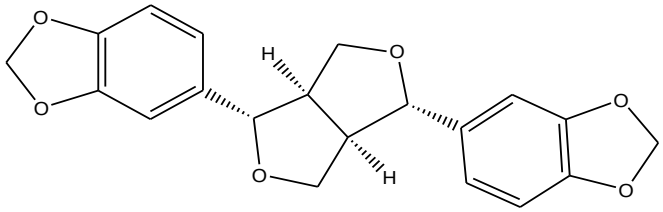
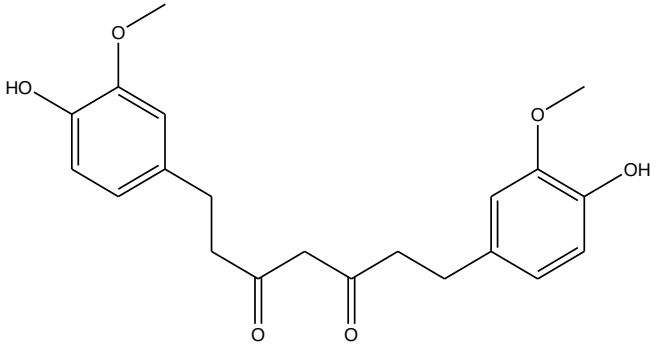
17.	Coenzyme Q10 303-98-0		Mitochondrial respirator chain component	Increased mean longevity by 18.0% when scavenging reactive oxygen species. [60]
18.	D-Glucosamine 3416-24-8		Hexosamine pathway	By controlling AMPK and SKN-1, researchers were able to achieve an 11.0 percent improvement in mean longevity while simulating a low carbohydrate diet.[61]
19.	Dimethyl sulfide 75-18-3		Metabolite of marine algae or fermentative bacteria	The average longevity has grown by 24.2 percent, as have antioxidant levels. [62]
20.	(-)-Epicatechin 490-46-0		Cocoa	The average lifetime has increased by 8%, indicating that more study is needed. [63]

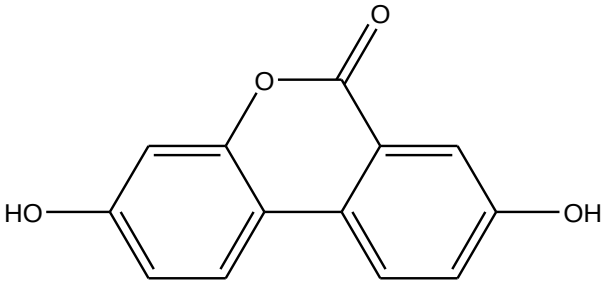
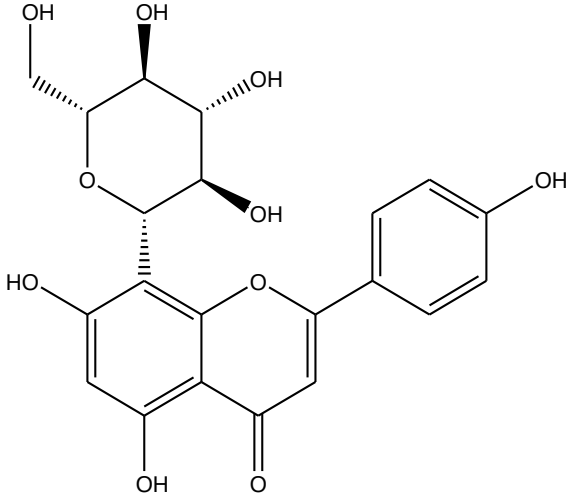
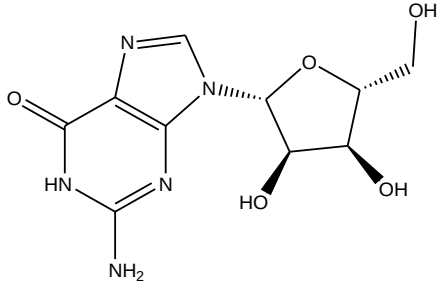
21.	Epigallo-catechin gallate 989-51-5		Polyphenols in tea	13.0 percentage increase in average antioxidant activity and lifespan, indicating that the IIS pathway is being regulated. [64]
22.	Gallic acid 149-91-7		Beverages	The average lifetime and antioxidant levels have increased by 25.0 percent. [65]
23.	Gluconate 527-07-1		Sugarsmeta bolite	The average lifetime and antioxidant levels have increased by 22.0 percent. [66]

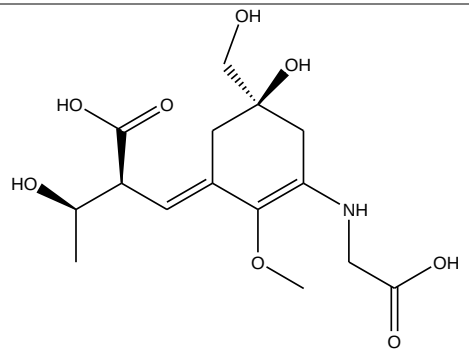
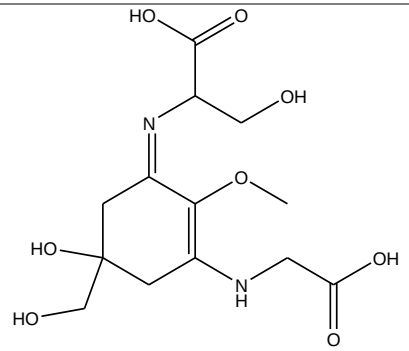
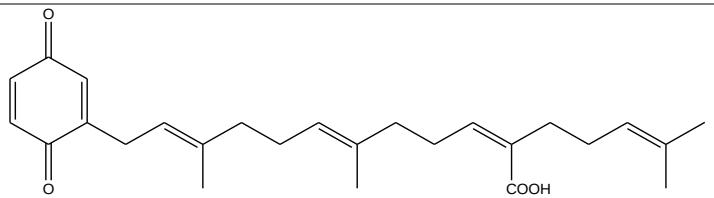
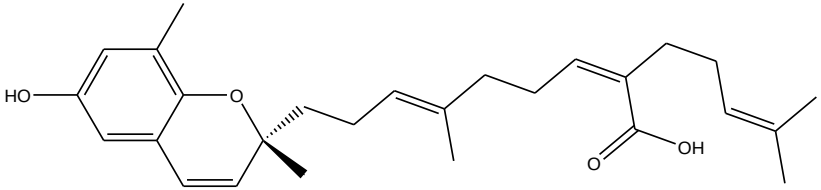
24.	Glycerol 56-81-5		Sugars metabolite	The average lifetime has increased by 21.0 percent, indicating that more study is needed.[67]
25.	Inositol 87-89-8		polyamines, phospholipid	C. elegans with nitrogen deficiency had a 17.0 percent increase in mean longevity and additional study is needed.[52]
26.	Hesperidin 520-26-3		Citrus genus	UTH1. regulates Sir2, resulting in a 37 percent increase in average lifespan and antioxidant.[68]

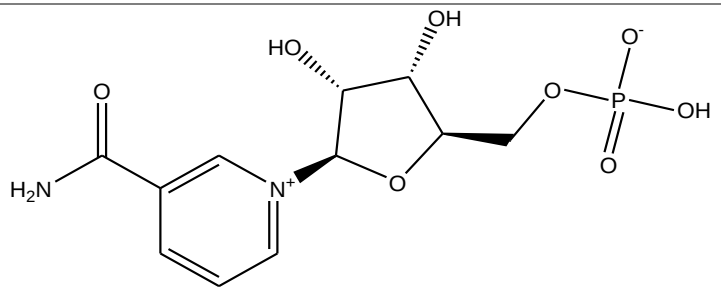
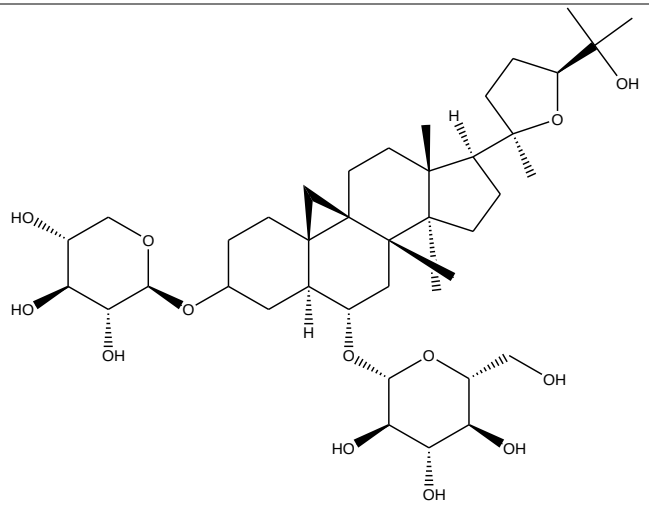
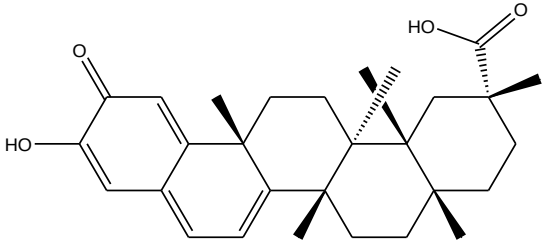
27.	Icariin 489-32-7		Herba epimedii	The IIS pathway is regulated, resulting in a 20.7 percent increase in average lifespan. [69]
28.	Arginine 74-79-3		Amino acid	Increased oxidative stress by 27.0 percent, heat stress by 370 percent, and antioxidant, which regulates the insulin/IGF signaling system. [70]
29.	Lactate 50-21-5		Metabolite	The average lifespan and antioxidant levels have increased by 15.0 percent. [66]
30.	Nordi-hydroguaiaretic acid 500-38-9		Creosote plant	The average lifetime has increased by 64.0 percent, indicating that more study is needed.[71]

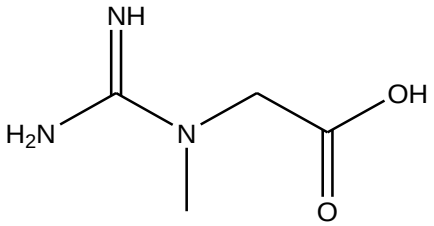
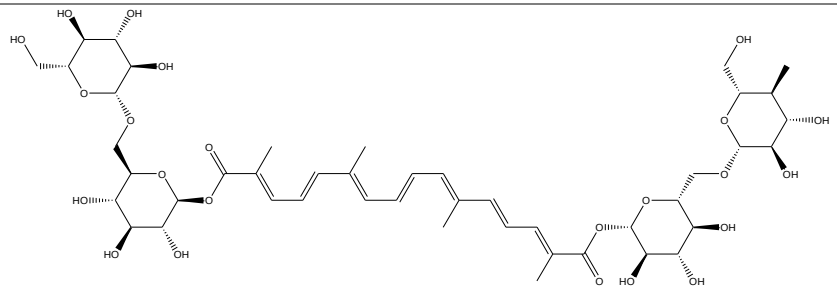
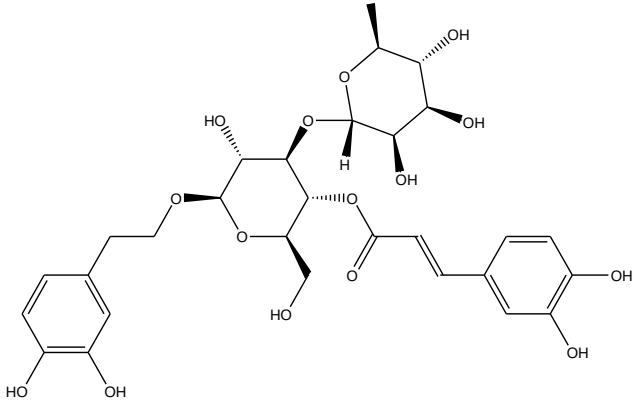
31.	Oleanolic acid 508-02-1		olive oil	DAF-16 regulates DAF- 16 percent increase in average lifespan and antioxidant.[72]
32.	Oligonol 851983-55-6		lychee fruit,	AMPK and autophagy regulation [73]
33.	Polydatin 27208-80-6		Grapejuice	SKN-1, DAF-2, SIR-2.1, DAF-16, and SOD-3 have been demonstrated to control each other., resulting in a 30.0 percent increase in mean lifetime.[74]

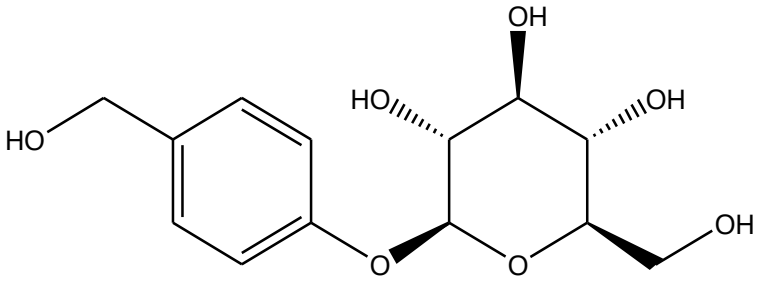
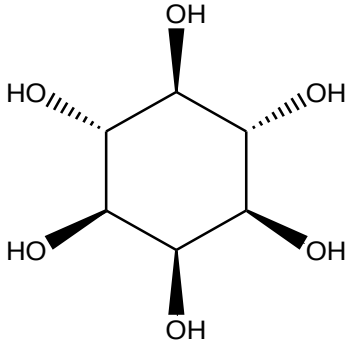
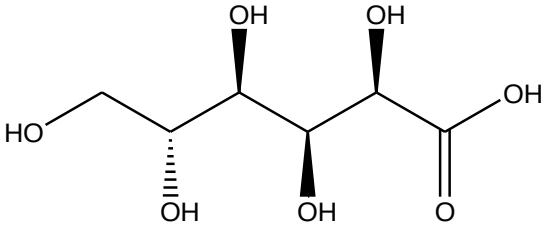
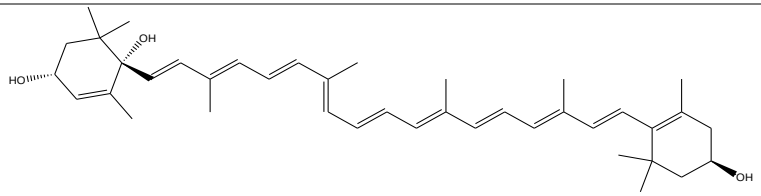
34.	Rosmarinic acid 537-15-5		Subfamily Nepetoideae of the Lamiaceae	DAF-16, SIR-2.1, SEK-1, UNC-43, and OSR-1 have all been demonstrated to control each other.[75]
35.	Sesamin 607-80-7		seeds of sesame	The average lifetime and antioxidant levels increased by 12.0%. [76] DAF-16, DAF-2, PMK-1, and SKN-1 are all regulated by DAF-16, DAF-2, PMK-1 and SKN-1.[77]
36.	Tetra-hydrocurcumin 36062-04-1		Curcuma longa	The average longevity has increased by 28.0%, and the average lifespan has been regulated. Fox O and Sir2.[78]

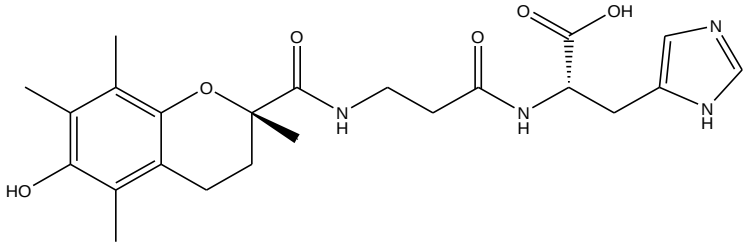
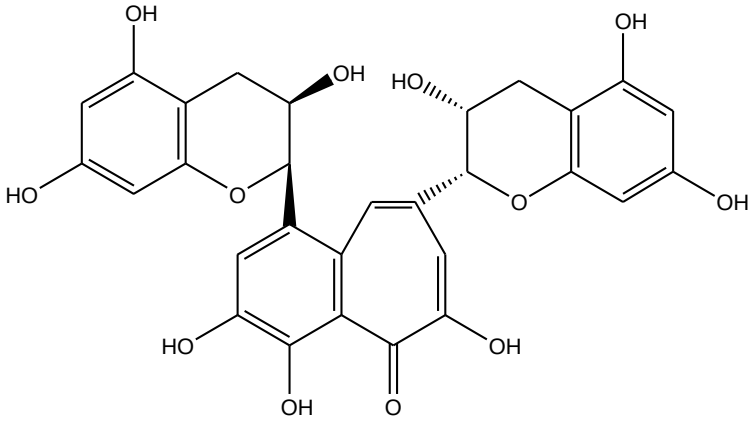
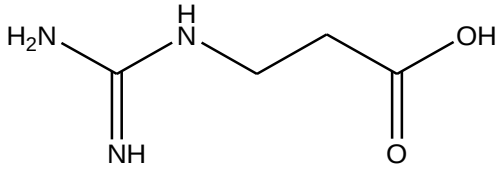
37.	UrolithinA 1143-70-0		Pistachios, brewed tea, blackberries	Mitophagy, a process that regulates mitochondrial activity, has increased the average lifetime by 45.4 percent.[79]
38.	Vitexin 3681-93-4		passion flower ,	There was a 17.0 percent increase in average longevity and antioxidants.[80]
39.	Guanosine 118-00-3		Endogenous nucleoside	Antioxidant is a term used by Wistarrats.[81]

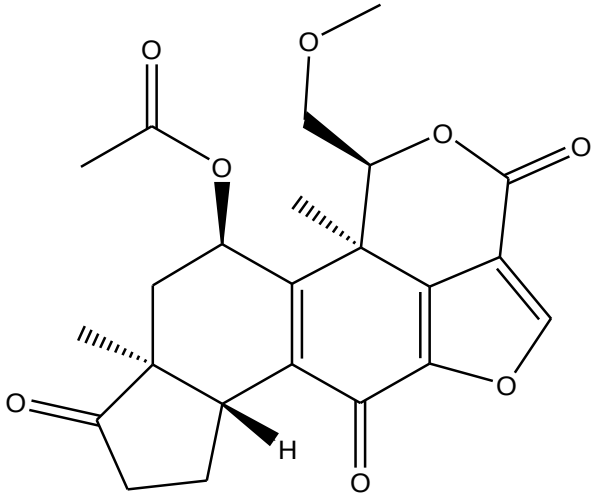
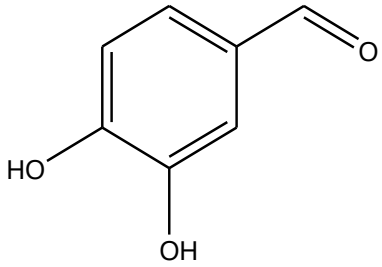
40.	Porphyra-334 70579-26-9		marine red algal species	In mice skin: antioxidant, Hsp70.[81]
41.	Shinorine 73112-73-9		Red alga Porphyra rosengurttii	Hsp70, antioxidant, inmiceskin.[82]
42.	Sargaquinoic acid 70363-87-0		sea holly, peat moss	Inducing apoptosis in miceskin.[83]
43.	Sarga-chromenol 70363-89-2		sea holly, peat moss	Apoptosis is induced by triggering apoptosis in mice.[83]

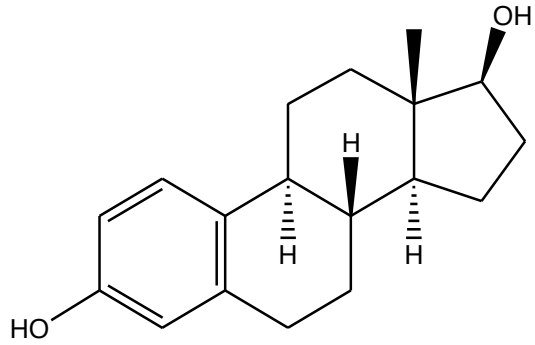
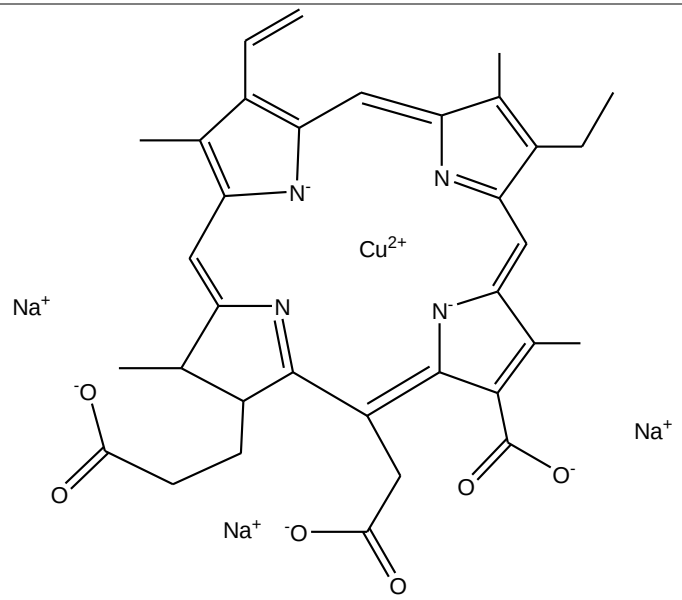
44.	Beta-Nicotinamide mononucleotide 1094-61-7		broccoli, cabbage	In rats, the amount of NAD+ is rising.[84]
45.	TA-65 1339070-29-9		Astragalus membranaceus	Telomerase activation in inmice.[85]
46.	Celastrol 34157-83-0		Tripterygium wilfordii	Increased mean life span by 13.0% and inhibited neuronal cell death via modulating HSP70. [86]

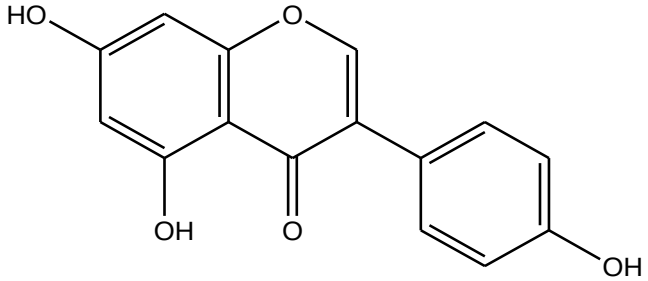
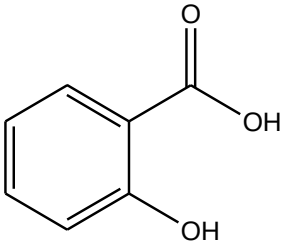
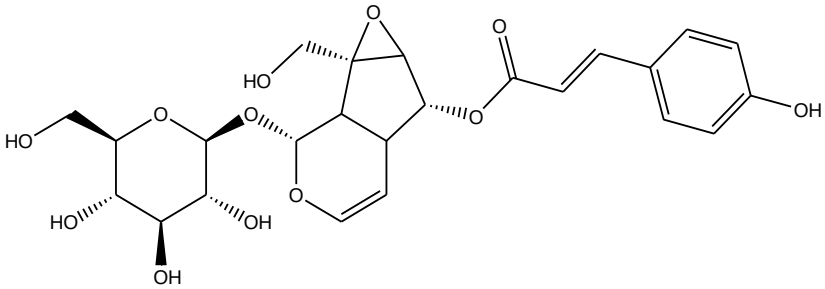
47.	Creatine 57-00-1		ergogenic compound	Upregulation of genes involved in neuronal development, neuroprotection, and learning resulted in a 9.0% increase in average longevity.[87]
48.	Crocin 42553-65-1		Kashmiri saffron	The average lifetime has increased by 44.0 percent, affecting haematological characteristics. [88]
49.	Acteoside 61276-17-3		Plantago ovata, Barleria lupulina	In a mouse model of aging produced by a mixture of D-gal and AlCl3, reducing nitric oxide, nitric oxide synthase activity, and caspase-3 expression.[89]

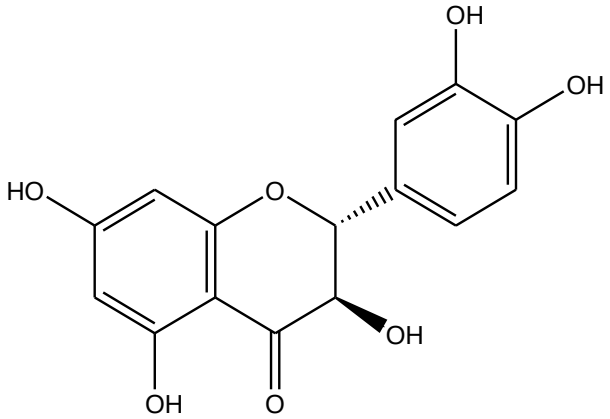
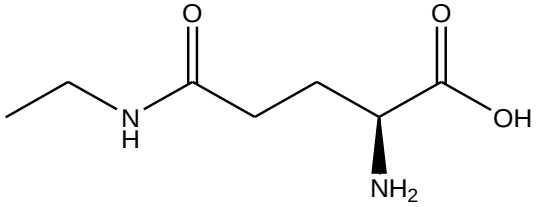
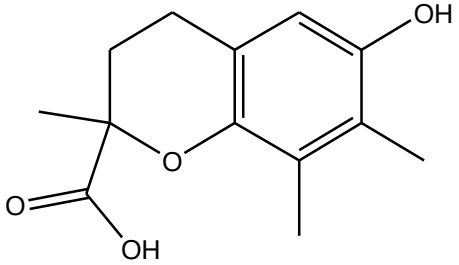
50.	Gastrodin 62499-27-8		orchid Gastrodia elata	In the case of vascular dementia, Chronic ischemia-induced rats: antioxidant, modulating ADH7, GPX2, GPX3, and NFE2L2.[90]
51.	Chiro-inositol 87-89-8		Inositol family	16.7 percent increase in average lifespan and antioxidant activity by modulating FOX O.[91]
52.	Gluconic acid 526-95-4		Glucose catabolism	The average lifetime and antioxidant levels have increased by 22.0 percent.[66]
53.	Lutein 127-40-2		Bell Peppers, Eggs, Corn	There was an 11.0 percent increase in average life span and antioxidants.[92]

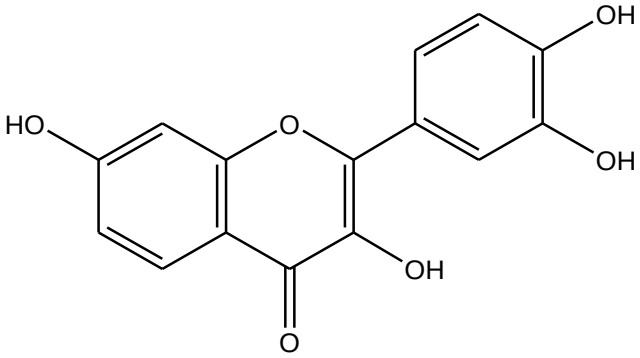
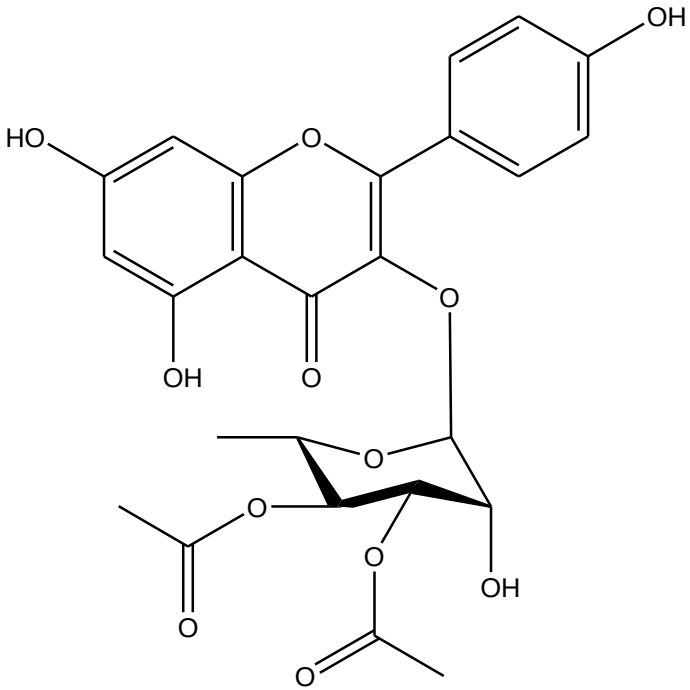
54.	S,S-Trolox-carnosine 1004313-10-3		Trolox acylated derivatives	The average lifetime and antioxidant levels have increased by 36.0 percent.[57]
55.	Theaflavins 4670-05-7		red tea	The average lifetime and antioxidant levels have increased by 10%.[93]
56.	b-Guani-dinopropioni c acid 353-09-3		Metabolites	Increased mean longevity by 13.0% in females and 90% in males by modulating AMPK Atg1-autophagy signalling.[94]

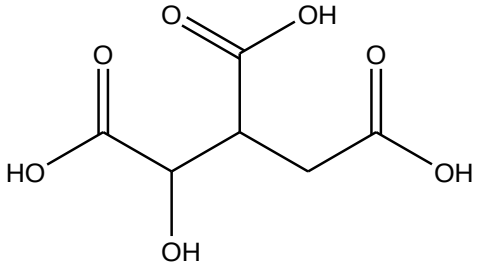
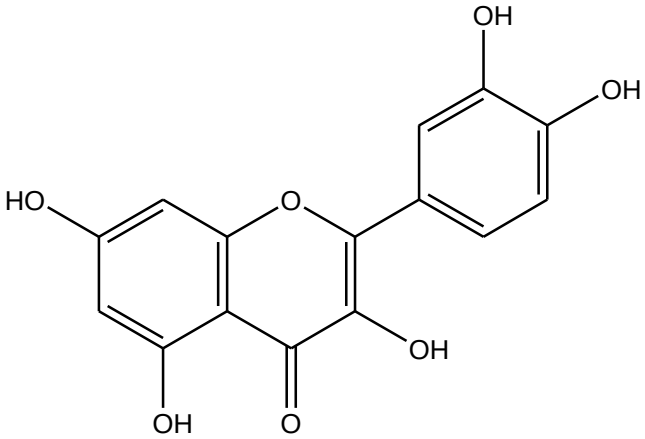
57.	Wortmannin 19545-26-7		Black spot of pineapple	A 5.0 percent increase in average lifetime and PI3K habituation.[95]
58.	3,4-Dihydroxybenzaldehyde 139-85-5		Sasa senanensis leaves	Prolyl 4-hydroxylase's 2-oxoglutarate binding sites were inhibited, resulting in a 23.0% increase in mean longevity.. [96]

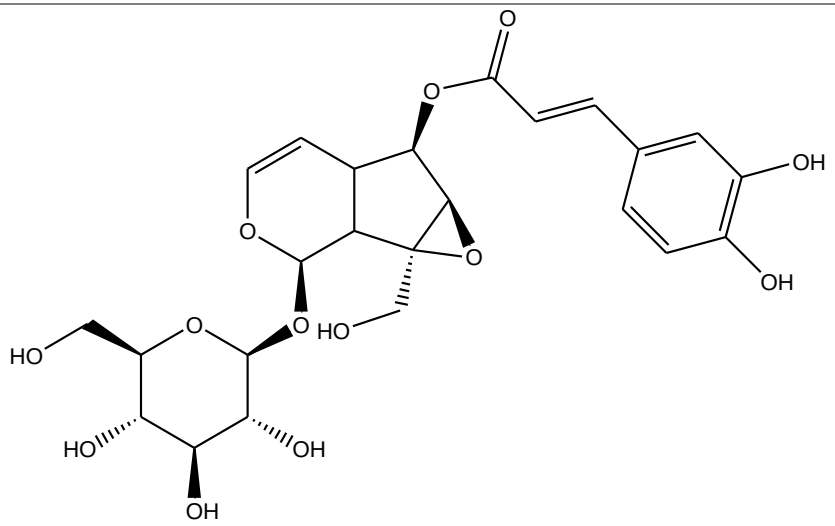
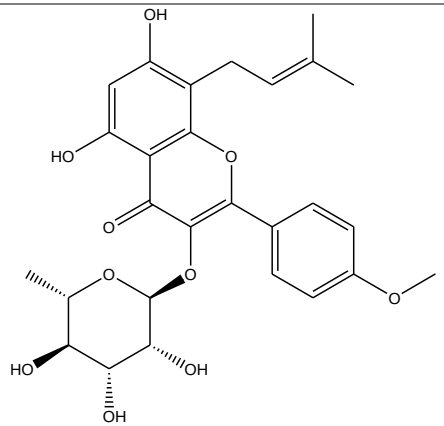
59.	Beta-Estradiol 57-91-0		Hormone	The average lifespan and antioxidant levels have increased by 7.0 percent. [97]
60.	Chlorophyll 1406-65-1		Vegetables (green)	25 percent increase in average life span and antioxidants.[98]

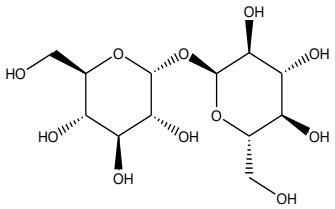
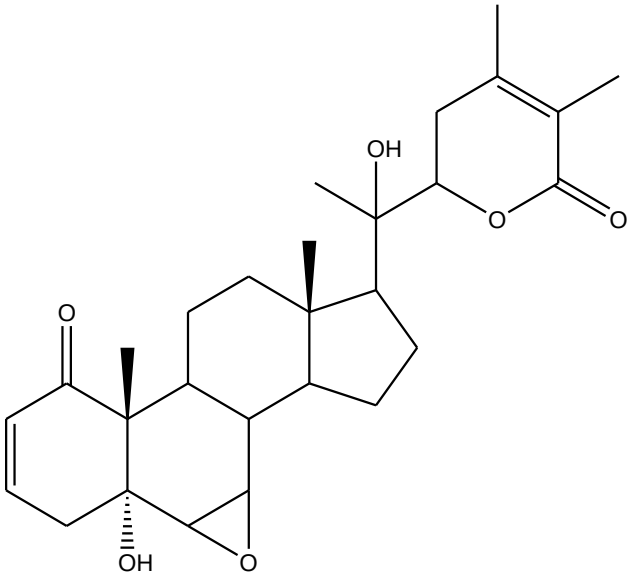
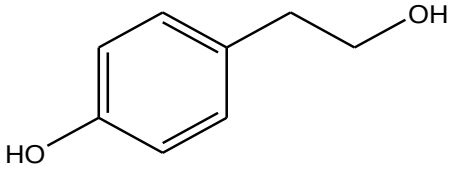
61.	Genistein 446-72-0		Vigna angularis	Antioxidant and mean lifetime increased by 27.9%.[100,101]
62.	Salicylic acid 69-72-7		Plant hormone	The average lifetime has increased by 14.0 percent, while antioxidant levels have increased by 14.0 percent.[102]
63.	Specioside 72514-90-0		Stereospermum suaveolens	The average lifespan and antioxidant levels have increased by 15.5 percent.[103]

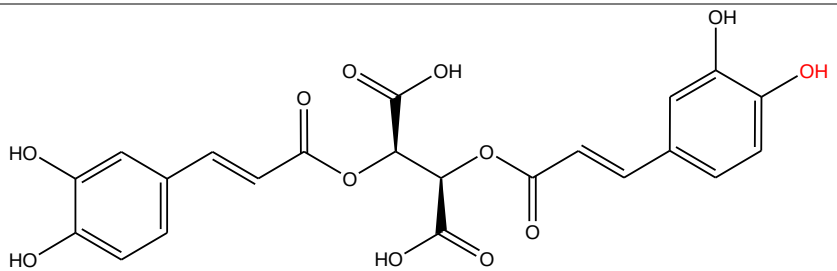
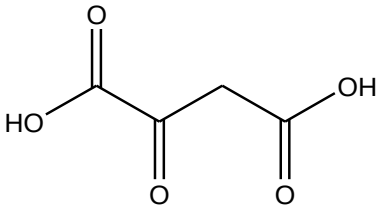
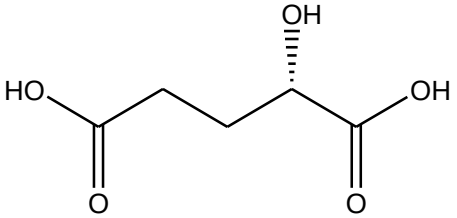
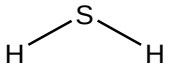
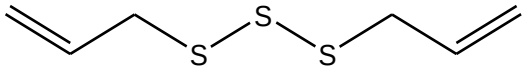
64.	Taxifolin 480-18-2		Citrus fruits and onion	The average lifetime has increased by 51.0 percent, while antioxidant levels have increased by 51.0 percent.[104]
65.	Theanine 3081-61-6		Camellia sinensis	An increase of 5.0 percent in average lifespan and antioxidants.[105]
66.	Trolox 53188-07-1		Vitamin E analog	The average lifetime and antioxidant levels increased by 31.0 percent.[104]

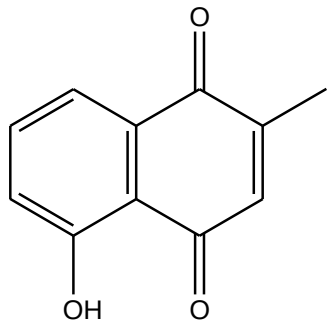
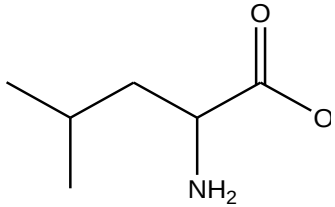
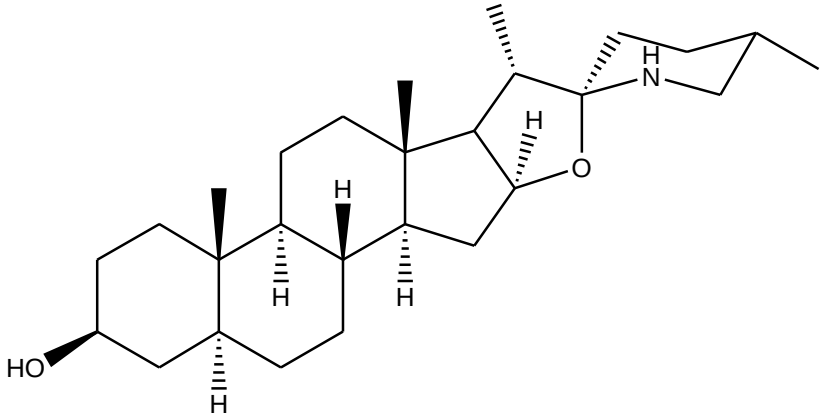
67.	Fisetin 528-48-3		Apples, onions, grapes, and a variety of other herbal foods	mechanical stress and antioxidant, controlling DAF- 16, had a 6.0 percent improvement in mean lifetime.[106]
68.	Kaempferol 520-18-3		Apples, onions, grapes, and a variety of other herbal foods	10 percent increase in average lifetime and antioxidant activity, as well as DAF-16 regulation.[106]

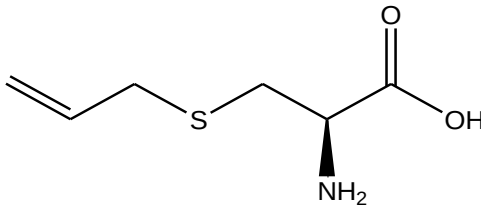
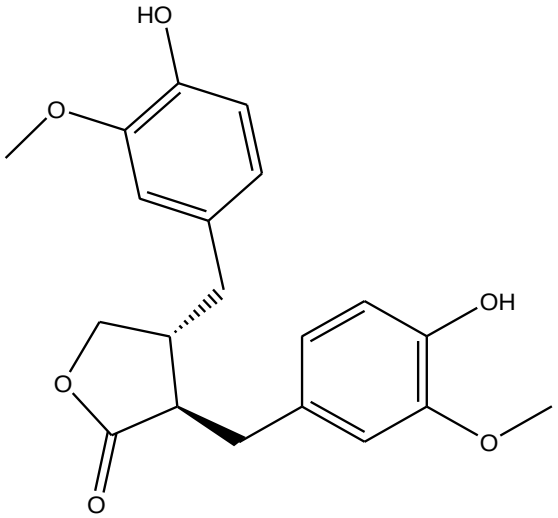
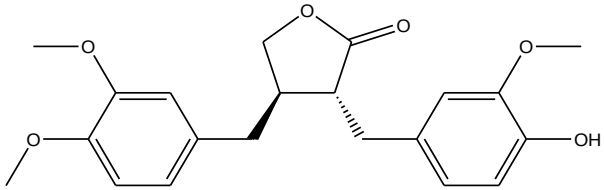
69.	Isocitrate 320-77-4		TCA cycle intermediate	There has been a 13.0% rise in the average longevity, and additional study is needed.[52]
70.	Quercetin 117-39-5		Red wine, tea, and Ginkgo biloba extracts, as well as onions, apples, and broccoli	15.0 percent increase in average lifespan and antioxidant activity, as well as DAF-16 regulation[107]

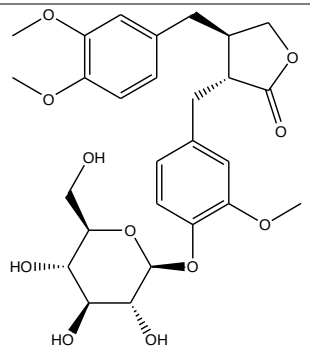
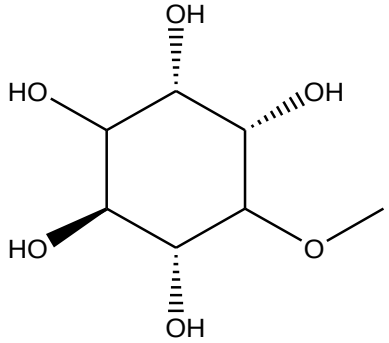
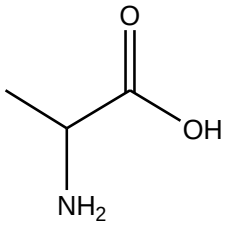
71.	Verminoside 50932-19-9		Stereospermum suaveolens	Antioxidant, controlling DAF-16, and 20.8 percent improvement in mean lifetime.[108]
72.	Icariside II 113558-15-9		Icariin active metabolite	Regulation of IIS signaling leads to a 20.0 percent increase in average lifetime.[69]

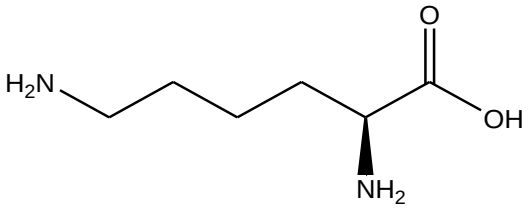
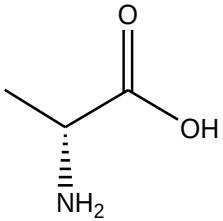
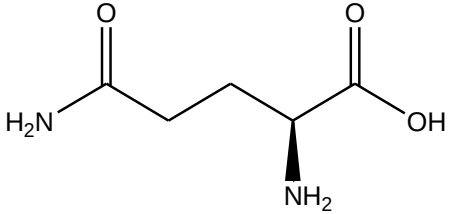
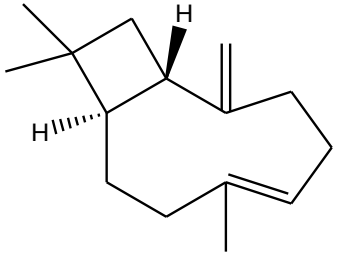
73.	Trehalose 99-20-7		Disaccharide of glucose	32.0 percent longer average lifetime and IIS signalling regulation.[109]
74.	Withanolide A 32911-62-9		Ayurvedic	The IIS pathway and brain activity were both regulated, resulting in a 29.7% increase in average lifetime.[110]
75.	Tyrosol 501-94-0		Extra virgin olive oil	The IIS pathway and the heat shock response were both regulated, resulting in a 10.8% increase in average longevity.[111,112,113]

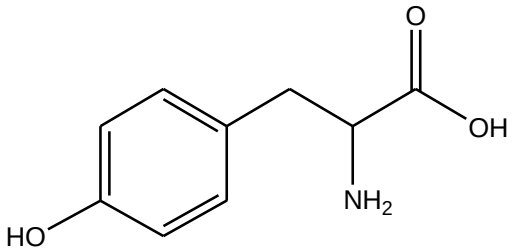
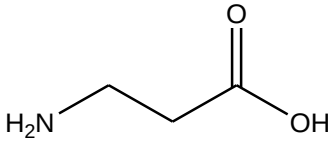
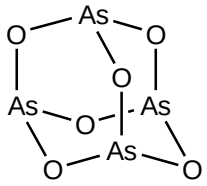
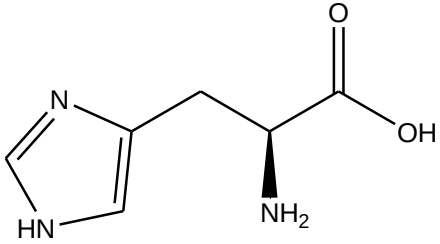
76.	Chicoric acid 6537-80-0		Caffeoyl derivative	AMPK regulation leads to a 21.0 percent increase in average lifespan.[115]
77.	Oxaloacetate 328-42-7		Metabolite of the citric acid cycle	Citric acid cycle metabolite increases mean lifetime by 25.0 percent while also regulating AMPK.[116]
78.	(S)-2-Hydroxyglutarate 13095-48-2		Oncometabolite	Citric acid cycle metabolite increases mean lifetime by 25.0 percent while also regulating AMPK.[116]
79.	Hydrogen sulfide 7783-06-4		Animal cells generate it naturally.	SIR-2.1. regulates SIR-2.1.118,119, resulting in a 74.0 percent increase in average lifespan and antioxidant.[118,119]
80.	Diallyl trisulfide		Garlic	12.6 percent longer average lifetime and SKN-1 regulation.[120]

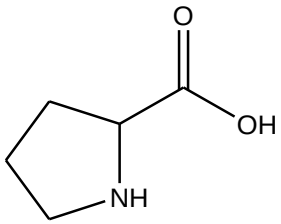
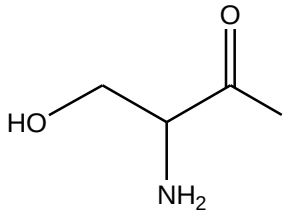
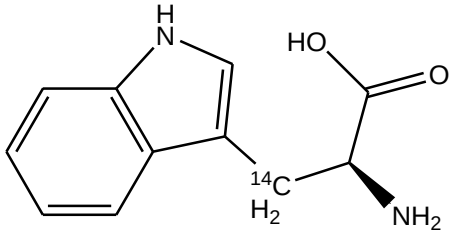
	2050-87-5			
81.	Plumbagin 481-42-5		Plumbago zeylanica L.	15.0 percent longer average lifetime and SKN-1 regulation.[121]
82.	Leucine 61-90-5		Amino acids	The regulation of SKN-1 and DAF-16 resulted in a 16.0 percent increase in average lifespan.[52]
83.	Tomatidine 77-59-8		Tomato fruits, leaves, and stems that aren't ripe	Mitophagy is regulated by the SKN-1/Nrf2 pathway, which results in a 7.0 percent increase in average lifespan.[122]

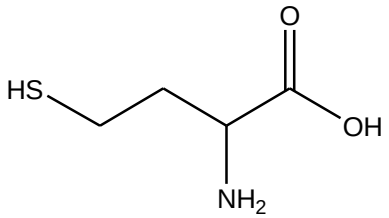
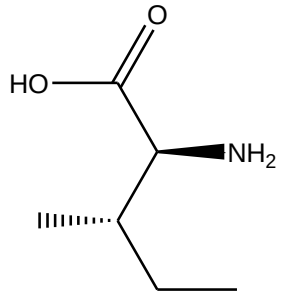
84.	S-Allylcysteine 21593-77-1		Allium sativum L.	SKN-1 regulates SKN-1, resulting in a 17.0 percent increase in average lifespan and antioxidant.[123]
85.	Matairesinol 580-72-3		Arctium lappa	Regulation of JNK-1 and DAF-16, resulted in a 25.0 percent increase in average longevity.[124]
86.	Arctigenin 7770-78-7		Arctium lappa	JNK-1 and DAF-16 are regulated, resulting in a 14.0 percent increase in average longevity and antioxidant activity.[124]

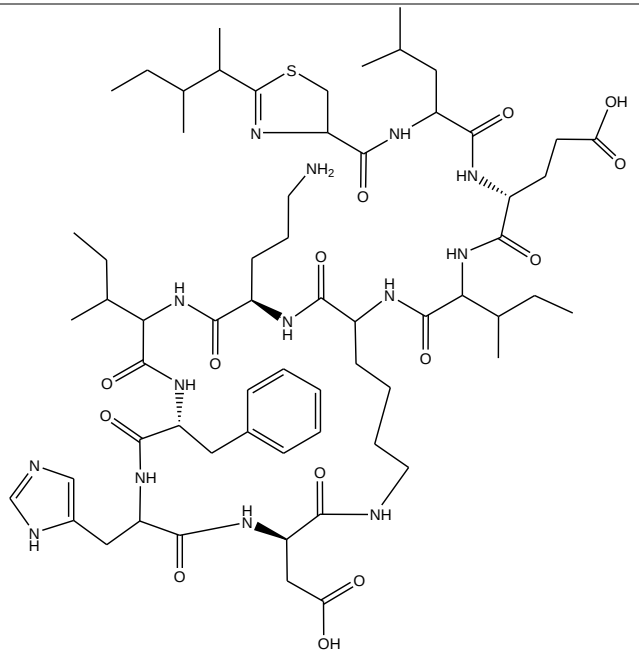
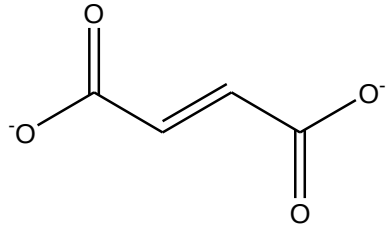
87.	Arctiin 20362-31-6		Arctium lappa	JNK-1 and DAF-16 are regulated, resulting in a 14.0 percent increase in average longevity and antioxidant activity.[124]
88.	Pinitol 484-68-4		Alfalfa, fine wood, and legumes	Regulation of JNK, S6K, and DAF-16. resulted in a 13.0% increase in average longevity.[91]
89.	Alanine 56-41-7		Amino acid	AAK-2, SKN-1, and DAF-16 regulate AAK-2, SKN-1, and DAF-16, resulting in an 11.0 percent improvement in average lifetime.[53]

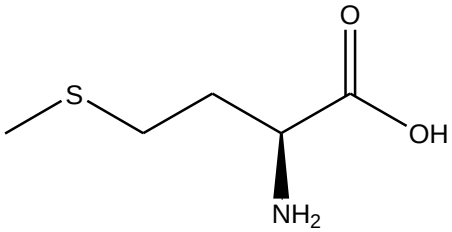
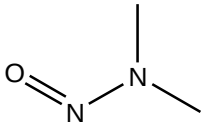
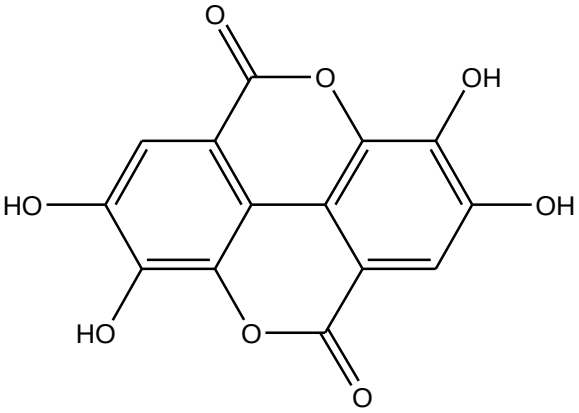
90.	Lysine 56-87-1		Amino acids	controlling AAK-2, SKN-1, and DAF-16 and increasing average lifetime by 8%.[53]
91.	D-Alanine 338-69-2		Amino acids	AAK-2, SIR-2.1, and DAF-16 regulate AAK-2, SIR-2.1, and DAF-16, resulting in a 16.0 percent increase in average lifetime. [53]
92.	Glutamine 56-85-9		Amino acids	EAT-2, AAK-2, and SKN-1 regulation resulted in a 16.0 percent increase in average lifespan.[53]
93.	B Caryophy Lene 87-44-5		Edible plants	SIR-2.1, SKN-1, and DAF-1 regulation resulted in a 22.0 percent increase in average lifespan.[125]

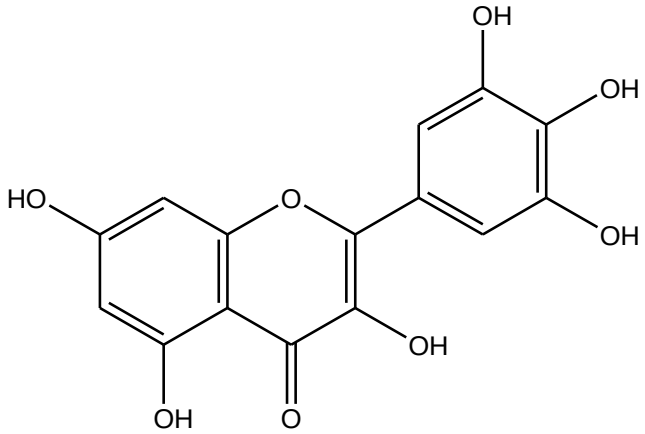
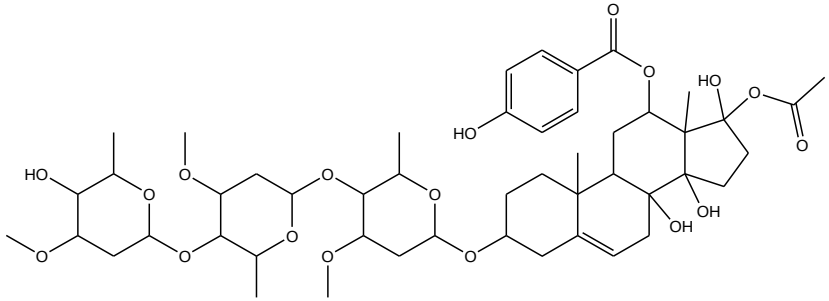
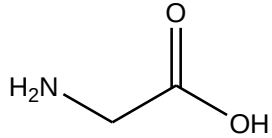
94.	Tyrosine 60-18-4		Amino acids	SIR-2.1, SKN-1, and DAF-16 regulate SIR-2.1, SKN-1, and DAF-16, resulting in a 10% increase in average longevity.[53]
95.	b-Alanine 107-95-9		Amino acid	AAK-2, SIR-2.1, SKN-1, and DAF-16 regulate AAK-2, SIR-2.1, SKN-1, and DAF-16, resulting in a 13.0% increase in average lifetime.[53]
96.	Arsenite 15502-74-6		Natural and anthropogenic sources	(10,000 lM) An increase of 10% in the average lifetime ([100 lM) 12.0% reduction in antioxidant activity and regulation of SKN-1, MTL-2, TIN-9, and DAF-16.[126,127]
97.	Histidine 71-00-1		Amino acids	Increasing the average lifespan by 12.0% and controlling EAT-2, AAK-2, SIR-2.1, SKN-1, BEC-1, HIF-1, GAS-1, IFE-2, GCN-2, and

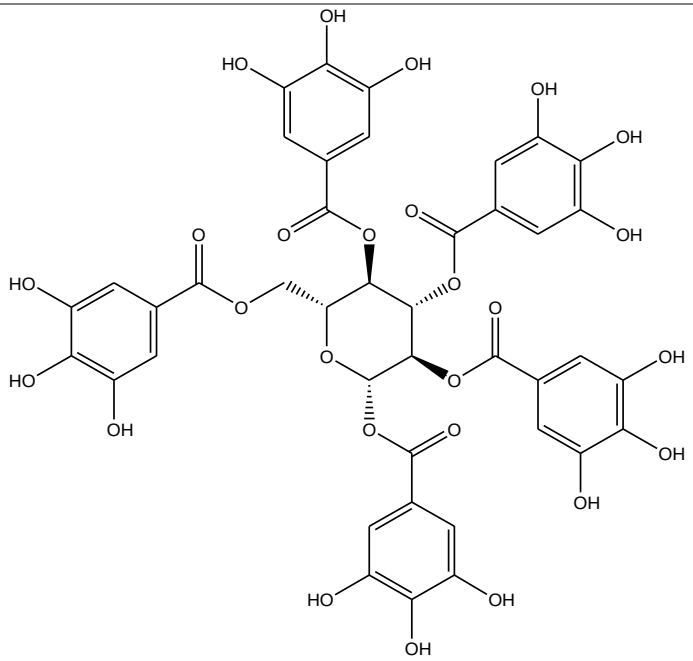
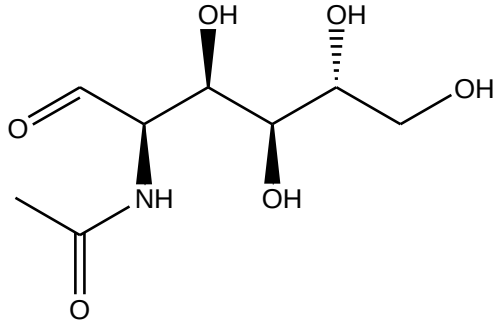
				DAF-16 are some of the genes that have been identified.[53]
98.	Proline 37159-97-0		Amino acids	Increasing the average lifespan by 19.0 percent and controlling EAT-2, AAK-2, SIR-2.1, SKN-1, BEC-1, and DAF-16 are some of the genes that have been identified.[53]
99.	Serine 56-45-1		Amino acids	Increasing the average lifespan by 22.0 percent and controlling EAT-2, AAK-2, SIR-2.1, SKN-1, HIF-1, BEC-1, and DAF-16 are some of the genes that have been identified.[53]
100.	Tryptophan 73-22-3		Amino acids	Increasing the average lifespan by 14.0 percent and controlling EAT-2, AAK-2, SIR-2.1, SKN-1, BEC-1, GCN-2, and DAF-16 are some of the genes that have been identified.[53]

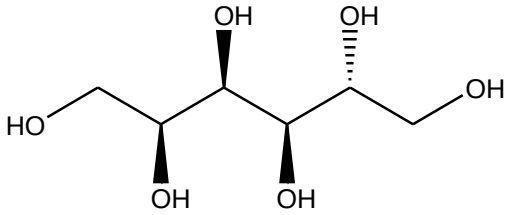
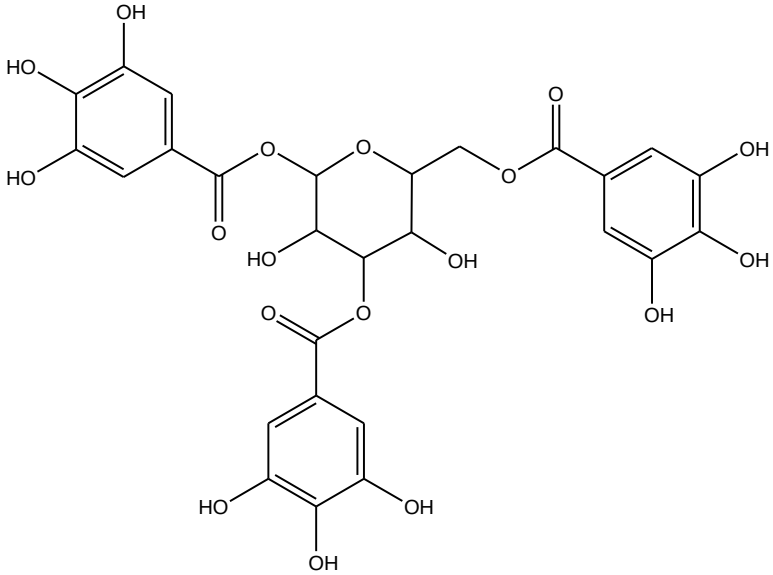
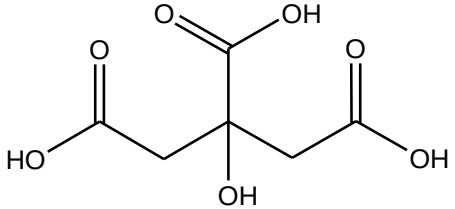
101.	Homocysteine 6027-13-0		Nitrogen containing metabolites	There has been a 13.0% rise in the average longevity, and additional study is needed.[52]
102.	Isoleucine 7004-09-3		Amino acids	There has been a 3.0% rise in the average longevity, and additional study is needed.[52]

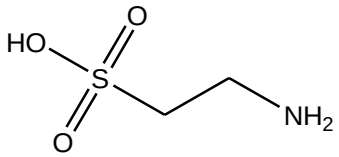
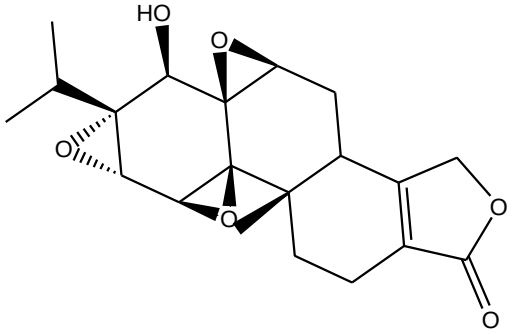
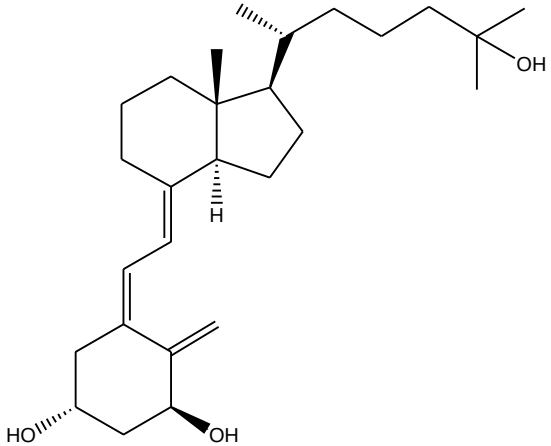
103.	Bacitracin 1405-87-4		Bacillus subtilisvar Tracy	Increased mean longevity by 59.0 percent and improved proteotoxcity through modulating CBP-1.[128]
104.	Fumarate 142-42-7		Tricarboxylic acid (TCA) cycle metabolite	Increased levels of oxidised NAD and FAD cofactors resulted in a 16.0 percent increase in mean lifetime.[129]

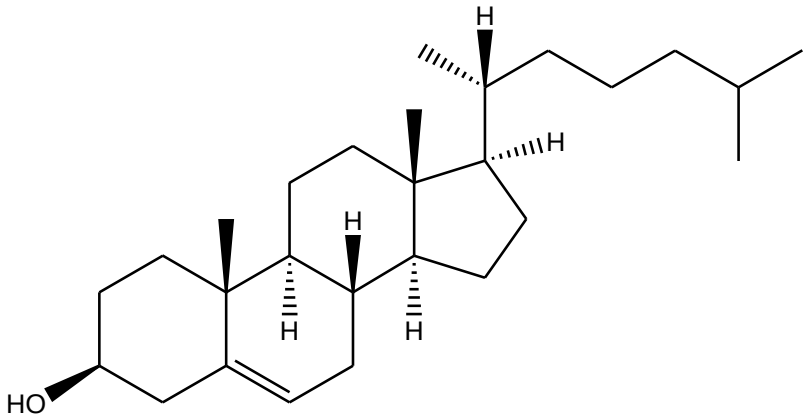
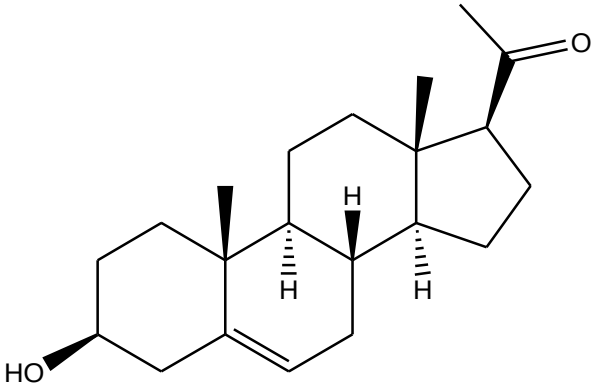
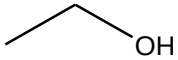
105.	Methionine 63-68-3		Amino acids	Regulation of mitochondrial unfolded protein response and a 14.0 percent improvement in mean lifetime.[52]
106.	N-Nitrosodimethy lamine 62-75-9		Organic xenobiotic substances that are widely distributed	a 6.0% increase in average lifespan and a decrease in the transcription of numerous stress response genes.[225]
107.	Ellagic acid 476-66-4		Strawberry and raspberry	Antioxidants, CR mimetics, and antimicrobials all contributed to a 10% increase in average longevity.[65]

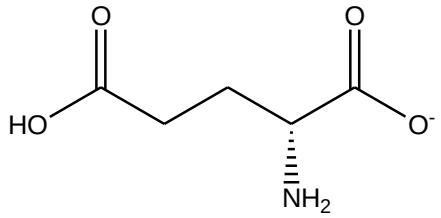
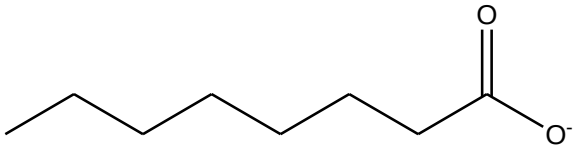
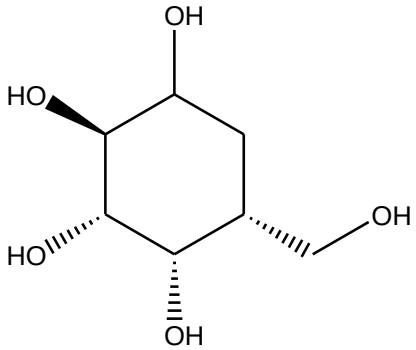
108.	Myricetin 529-44-2		Tea, various vegetables, onions, berries, grapes, and medicinal plants are just a few examples.	34.3 percent longer average lifespan and DAF-16 regulation; improved quality of life as people age.[47,131]
109.	Otophyllosid e B 106758-54-7		Cynanchum otophyllum	DAF-2, SIR-2.1, CLK-1, and DAF-16 regulate DAF-2, SIR-2.1, CLK-1, and DAF-16, resulting in an 11.3 percent increase in mean lifetime.[132]
110.	Glycine 56-40-6		Amino acids	The average longevity has increased by 10%, and additional study is needed.[52]

111.	Pentagalloyl glucose 14937-32-7		Eucalyptus leaves	Dietary restriction, the IIS pathway, SIR-2.1, and the mitochondrial electron transport chain all contributed to an increase in mean longevity of 18.0%.[133]
112.	N-Acetyl-glucosamine 7512-17-6		Hexosamine Pathway Metabolite	Autophagy, ER-associated protein degradation, and proteasomal activity were all improved, resulting in a 50.0 percent increase in mean lifetime.[134]

113.	Sorbitol 50-70-4		S. cerevisiae	DR and osmotic response regulation resulted in a 35.0 percent increase in mean longevity.[135]
114.	Tannic acid 1401-55-4		Grapes and green tea	TGF-b, p38 MAPK pathways, and DAF-12 regulation resulted in a 19.0% increase in mean lifespan.[136,137]
115.	Citrate 77-92-9		Tricarboxylic acid cycle intermediate	Increased mean lifetime by 13.0% while also activating the ER stress response.[52]

116.	Taurine 107-35-7		Nitrogen containing metabolites	Increase in average lifetime of 11.0 percent and induction of the ER stress response.[52]
117.	Triptolide 38748-32-2		Tripterygium wilfordii	HSP16.2 and SOD-3 regulate HSP16.2 and SOD-3, resulting in a 20.1 percent increase in average lifetime.[53]
118.	Vitamin D3 67-97-0		Vitamins	SKN-1, IRE-1, XBP-1, DAF-12, and proteostasis are all regulated by SKN-1, IRE-1, XBP-1, DAF-12, and proteostasis.[53]

119.	Cholesterol 57-88-5		Cyclo-pentanoper-hydro-phenanthrene ring	Cholesterol-binding protein regulation DAF-16 and NSBP-1.[139]
120.	Pregnenolone 145-13-1		Hormonal steroids	Linked to germline-defective controlled longevity, there was a 20.0 percent increase in mean lifespan.[140]
121.	Ethanol 64-17-5		Metabolites	Serving as a source of carbon and energy, as well as causing a stress reaction.[141]

122.	D-Glutamate 6893-26-1		Amino acids	The average lifetime has increased by 18.0–114.0 percent, and additional study is needed.[52]
123.	Caprylate 74-81-7		Metabolites	C. elegans with nitrogen deficiency had a 7.0 percent increase in mean lifetime, which warrants additional investigation.[142]
124.	Galact-opyranose 10257-28-0		Sugars metabolites	C. elegans with nitrogen deficiency had a 6.0 percent increase in mean longevity, and additional study is needed.[52]

4. CONCLUSION

Aging can be defined operationally as a time-dependent loss of fitness that begins to manifest after the organism attains its maximum reproductive competence. Assuming that aging is not the result of a pre-programmed set of events, as now seems clear. Phytochemicals derived from plants have a lot of Anti-aging beneficial properties related to UV protection, antioxidant action, matrix protection. Over the past decade, a lot of phytochemicals from the plant extracts have been explored and their biological activities well-studied in vitro. Therefore, there is a continuous requirement for more clinical studies with emphasis on the concentration of the ingredient in natural products, their formulation, safety, and the anti-ageing effect duration.

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