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A COMPREHENSIVE REVIEW OF PHARMACODYNAMICS, THERAPEUTICS, AND PHYTOCHEMICAL VALIDATION OF RASAYAN HERBS IN AYURVEDA

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ABSTRACT

Ayurveda has established a unique concept called *Rasayana* therapy, and is include in Ayurveda as it's eight division (*Jara vidnyan*). Due to several atmospheric factors, changed lifestyle, altered daily routine, work overload, stress, poor dietary habits, sedentary lifestyle, lack of exercise and metabolism, etc. there has been increased occurrence of various diseases such as Diabetes Mellitus, Cardiac diseases, nephrotic diseases, etc. *Swastharakhshan* and prevention of diseases (*vyadhi parivarjan)* is the motto of Ayurveda and the unique concept of *Rasayana* therapy is one among the curative factors for such increasing disorders. *Rasayana* name itself explains it's a role of *Rasadi dhatu ayana karma* i.e. *Rasadi dhatu* restoration or rejuvenation thereby reducing imbalance in *doshas* and restoring body equilibrium which can be explained as Health. *Rasayana Karma* occurs by the use of various plant medicine and has been in practice since ancient times. The Mode of action of *Rasayana dravyas* according to their *Rasa, Guna, Virya Vipak, Prabhav*, etc. are explained and a correlation between the factors occurring during increased metabolism and cellular restoration can be explained with the help of enormous physiological factors with validation from recent scientific researches. The *Rasayana karma* is explained with the help of various Ayurvedic concepts and supported and validated with the help of various pathophysiological and pharmacological actions obtained by these *Rasayana dravyas*.

KEYWORDS: Rasayana, Oxidative stress, free radicals, antioxidants, Anti-ageing.

INTRODUCTION

Ayurveda, is a natural health System and also the study of life. Through of progression in medical science in the form of inventions have been occurring manifold, like investigation contrivance and profound acquaintance of human physiology, etc. Simultaneously manifestation of newer health challenges are also emerging, which may be due to human lifestyle error or natural disasters. There has been no significant rheostat over these upcoming medical pandemics or diseases, rather newer lifestyle, metabolic, genetic, or environmental health grievances are emerging, many of them are without any remedy.

'Conserving the health of healthy and treating the disease of ill persons' is the first objective[1]of health-care plans before the treating any disease as per Ayurveda.

Rasayana is one of the comprehensive discipline of Ayurveda which comprises specialized use of herbs, herbomineral formulations, diet and lifestyle along with self-discipline, social etiquette to achieve the equilibrium of Dosha-Dhatu-Mala of our body[2] and optimum state of tissue and systems of our body to minimize the effects of etiological factors on the body.

For the conservation of equilibrium of these doshas and health, thereby prevention of diseases and premature ageing Ayurveda[3] has delineated the concept of Rasayana.

जरा व्याधि नाशकम् औषधम् रसायनम्। (च.चि. १/१-२)

Rasayanas are described as - the destroyers of senility and diseases.

- श्रेष्ठानाम् रस रुधिरानाम् यो लाभ उपायो रसायनम् उच्यते। (अरुणदत्त)

  Rasayanas are considered as Sources for best quality dhatus or tissues.

- रसायनम् च स्वस्थ आतुर विषयम् जरा च व्याधिः च तत् विध्वंसितुं शीलम् यस्य तद्रसायनम् इति। (शिवदास सेन)

Rasayanas are both preventive & curative medicines. *Rasayana dravyas* are the herbs that destroys the disproportion of the *Dosha-dhatu-mala* of the body, management of diseases, serving as the source of preeminent quality (*prasadbhut*) of *dhatus* and tissues.

METHODOLOGY

All the Information related to the *Rasayan dravyas* was collected from various Ayurvedic texts, *Samhitas*, and also various research articles related to Rasayana including Pubmed, Scopemed, Pubmed Central Databases, Dhara online database and other allied databases were studied for coleection of data and were referenced in this article.

Various modern concept such as Antioxidants, Reactive oxygen species, oxidative stress, rejuvenation, cardiac related disorders, urinary system related disorders , etc were reviewed and referenced to correlated and explain the *Rasayana* concept with the help of published and available research.

Why Need of Rasayana??

1) **Modernization**[4]- Factors such as continuous exposure to sunlight, radiation, pollution, chemical exposure, alcohol consumption, tobacco, smoking, obesity due to lack of exercise by the replacement of physical work with use of machines, unbalanced diet, excessive exercise for dieting, etc. leads to some kind of changes to human body and causes various physiological and cellular changes in our body leading to disruption of Body equilibrium and damage to cells reducing body build, immunity and various diseases occur which droves the body towards senility like factors leading to numerous metabolic disorder which consequently leads to shorter life span.
2) **Newly emerging pandemics**[5] and post pandemic health effects are also factors of great concern and needs to enhance the immunity and susceptibility turn out to be the priority. Recently the world has gone through the one of the most hazardous pandemic Covid-19. Even after treating the disease, it hampered our immunity and left with many complicated health issues. Also Covid-19 vaccination[6] which has been injected on large scale to take an effective action against Covid-19. But lately Various post vaccination complications like Neurological complications i.e. Intracerebral hemorrhage, ischemic stroke, encephalopathy, epilepsy, delirium, seizures, bell's palsy, optic neuritis, tinnitus and vascular complications like thrombocytopenia, venous sinus thrombosis, etc. emerged which proved to be rather more fatal.

Also disease like monkey pox, Mucormycosis have emerged as post Covid-19 complications which emphasized that merely cure for newly emerging diseases is not sufficient but boosting of one's own immunity has become crucial in today's era to safeguard ourselves from such hazardous pandemics which may help fight against such type of invasive pathogens causing various types of diseases.

3) Stress factors[7]

Emerging technologies have brought with it various stress factors like education, career, personal, work stress, etc. have led to declined, immunity of body due to imbalance in Trigunas i.e. Satvadi gunas which are correlated with shariar Doshas i.e Tri dosha, leading to doshs vaishamya i.e. is called as a *Vyadhi* or diseases.

4) Drastic changes in atmosphere[8]

Factors such as global warming, industrial resolution, increased temperature there is alteration of sequence of winter, summer and rainy season it also put great impact on health.

Altered atmospheric changes or seasons like seasonal variations have led to vitiation of various Sharira and Manas guns thereby resulting in mental and physiological changes and thereby various diseases. Janapadodhvansa[9] is the factor which is also responsible for manifestation of various diseases.

These factors altogether contribute to the increased Oxidative Stress and increased formation of free radicals, these molecules are generated through various endogenous processes like mitochondrial respiration and immune cell activation and also through exogenous sources.

These free radicals[10,11] are essential for numerous biological processes like cell signaling and immune defense but their overproduction can disturb the delicate balance between oxidants and antioxidants, leading to oxidative stress. Oxidative stress grounds the damage of critical biomolecules like DNA, proteins, and lipids, subsidizing to the pathogenesis of various chronic diseases such as cancer, cardiovascular diseases, neurodegenerative disorders, and inflammatory diseases which have strong connotation with the harmful effects of free radicals.

Effect of increased Oxidative Stress: Oxidative stress[12] is an imbalance of free radicals and antioxidants that leads to cell damage. It plays a role in many conditions like cancer, Alzheimer's disease and heart disease.

The cells produce free radicals during normal metabolic processes. However, cells also produce antioxidants that neutralize these free radicals. In general, the body is able to maintain a balance between antioxidants and free radicals.

Many diseases are linked to Oxidative Stress,[13] including diabetes mellitus inflammation, cancers, autoimmune disorders and various neurodegenerative diseases. More recently, substantial advances in biochemistry and molecular biology have empowered scientists to find master switches of various OS mechanisms and associate OS development too many biological archetypes. In this review, a brief summary of free radicals and Oxidative Stress related molecular mechanisms and their role in the progression of many disorders is emphasized. Likewise, more research is required to assess the utility of reactive oxygen species and their markers as a diagnostic tool.

What is Free radical?

Free radicals including reactive oxygen species,[13] such as – superoxide, hydroxyl radical, nitric oxide radical, etc. are the molecules with one or more unpaired electron in its outermost shell of cells having a tendency of combining with other freely available molecules.

Cell mitochondria generates energy in the form of adenosine triphosphate (ATP), during this process, mitochondria combine oxygen and glucose to produce carbon dioxide, water, and ATP, free radicals are also produced as byproducts of these metabolic processes.

Free radicals are oxygen-containing molecules with an uneven number of electrons which allow these free radicals to react easily with other body molecules and can form large chain chemical reactions in our body because they react very easily with other molecules, these reactions are called oxidation.

What is Anti- oxidant?[14]

Anti-Antioxidants are the substances that help neutralize or remove free radicals by donating an electron, this neutralizing effect of antioxidants helps safeguard the body from oxidative stress.

What are the effects of oxidative stress on Human Health?

Many of the recent scientific researches proved that oxidative stress is associated with the progression of major various diseases by inactivating the metabolic enzymes and damaging important cellular components, oxidizing the nucleic acids, leading to numerous diseases such as cardiovascular diseases, eye disorders, joint disorders, neurological diseases (Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis), atherosclerosis,

lung and kidney disorders, cancer, ageing, disease of the reproductive system including the male and female infertility etc.

Relation of Oxidative stress and cardiovascular system diseases[15,16,17,18]

Reactive oxygen species (ROS) at physiological level functions (normal levels) as signaling molecules to regulate wide range of processes in the cardiovascular system and to subsidize to the maintenance of homeostasis of cardiovascular system.

But when there is excessive or sustained increase in ROS generation it plays a crucial role in the instigation and progression of Cardiovascular Diseases.

Excessive levels of ROS cause damage to cellular[19] macromolecules such as DNA, lipids and proteins, ultimately causing necrosis and apoptotic cell death such as in CVD which is a generally occurring conditions due to increased oxidative stress. Increased ROS causes decreased nitric oxide availability and leading to vasoconstriction and thus promoting arterial hypertension. ROS also decreases the myocardial calcium management, causing arrhythmia, and increase cardiac restoration by inducing hypertrophic signaling and increased cell apoptosis. ROS also promotes atherosclerotic plaque formation, thus ROS is the major contributing factor of Cardiac disorders.

Relation of Oxidative stress and neurodegenerative diseases[20,21]

Neurodegenerative diseases such as Alzheimer Disease AD, Parkinson's Disease PD, Huntington's disease and Amyotrophic Lateral Sclerosis shows similarity in aggregation of disease-specific proteins in the CNS. Protein aggregation occurs in AD, due to the accumulation of abnormally folded beta-amyloid (Aβ) and tau proteins in the brain. Under normal conditions, a transmembrane protein amyloid-β precursor protein (AβPP) is required for neuron growth, survival and post-injury repair. However, in AD, APP is cleaved or chopped by some enzymes through proteolysis into a small peptide, 39–43 amino acids in lengthwise manner which is called Aβ. Aβ forms clumps and these deposits outside neurons in dense formations known as senile plaques and also phosphorylation of Tau protein results in abnormal aggregation and dysfunction of this protein in AD.

In PD, the protein alpha-synuclein (αSyn) binds to ubiquitin and forms proteinaceous cytoplasmic inclusions, Lewy bodies. Over accumulation and posttranslational modification of αSyn results in death of dopaminergic neurons.

Humans have two copies of the huntingtin gene (htt), which codes for the protein huntingtin (Htt), the mutant huntingtin protein (mHtt). During the natural clearance process of cells, these proteins are retrogradely circulated in body cells for destruction by lysosomes.

Under pathological conditions, these aggregated mutant proteins damage the retrograde transport of important molecules causing pathological changes and disease symptoms such as destruction of motor neurons due to proteinaceous inclusions in the cell bodies and axons of motor neurons. Protein degradation pathways play a crucial role in eradicating these aggregated proteins, thus increased oxidative stress alters these processes leading to such diseases conditions.

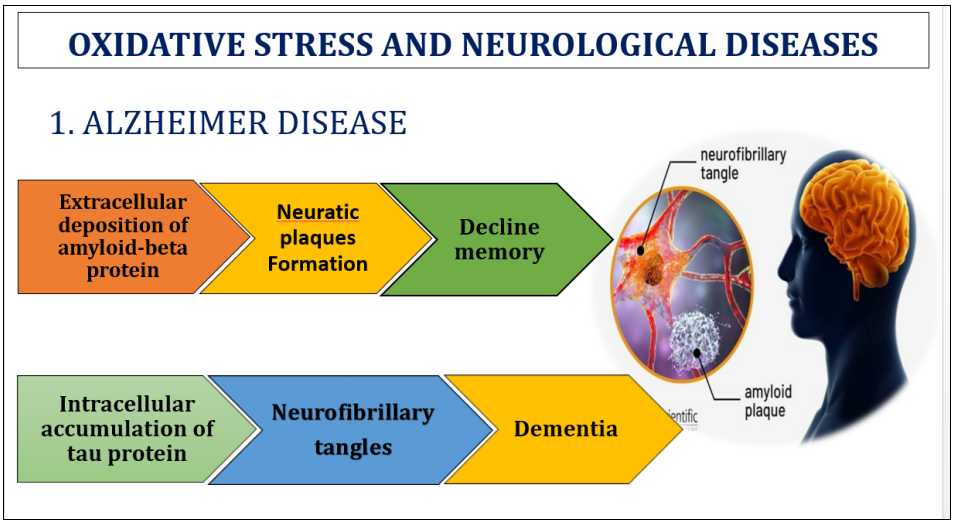


Figure 1: Schematic representation of correlation between correlation of oxidative stress and neurological diseases.

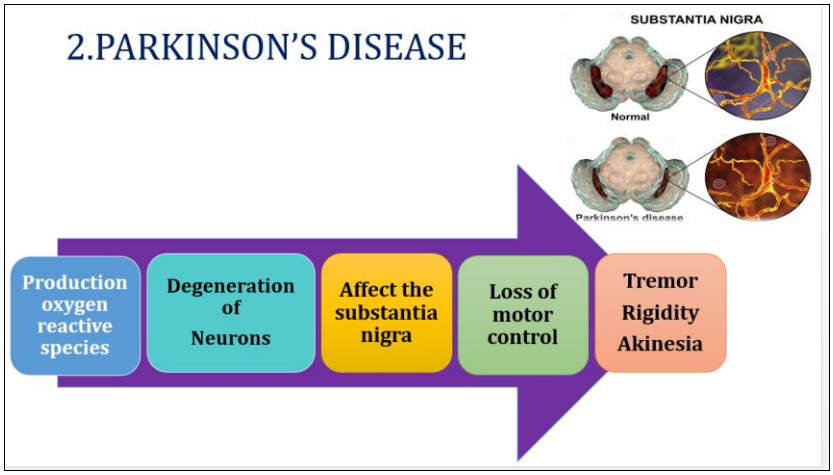
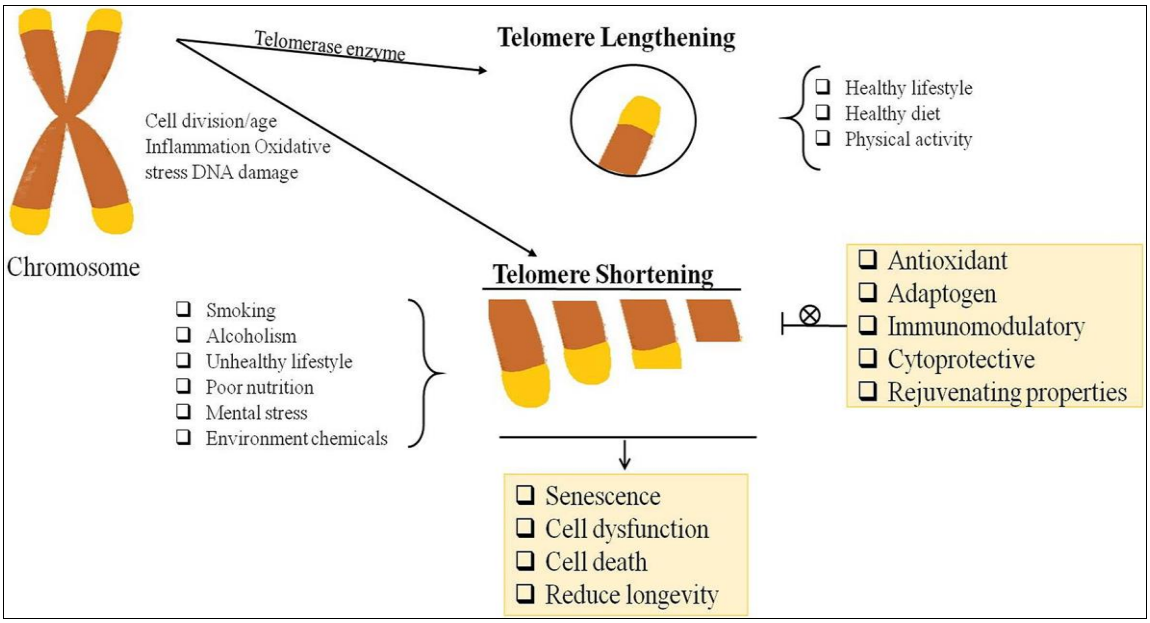


Figure 2: Schematic representation of correlation between oxidative stress and neurological diseases.

Effect of ROS and free radicals o telomere[22]



Source: Kirti Raina, Ruchika Kumari, Palak Thakur, Rohit Sharma, Randeep Singh, Abhinay Thakur, Vikas Anand, Rohit Sharma, Mechanistic role and potential of Ayurvedic herbs as anti-aging therapies, Drug Metabolism and Personalized Therapy

DNA damage can accelerate the aging by causing impact on transcription[23], signaling apoptosis or cellular senescence, telomere shortening. Telomere shortening causes telomere malfunction such as chromosome uncapping and activation of DNA damage leading consequently in causing the breakdown of a cell cycle and replication. The DNA's capacity of replication is hampered causing damaged DNA and thereby chromosomal damage leading to no new cell cycle and cell apoptosis.

Relation of OXIDATIVE STRESS AND RESPIRATORY DISEASES[24]

DNA Damage

There are several mechanism by free radicles that causes damage to DNA hydroxyl radicals produced in this reactions lead to distractive changes in the DNA structure caused by the reaction with is constituent parts like deoxyribose, purines and pyrimidine.

DNA damage assessment methods

There are many different methods for examining the extent of DNA damage. Single cell electrophoresis (comet assay) is one of the most common methods for assessing damage to DNA as well as assessing the strength of antioxidant compounds. In this method, the DNA which is having the ability to remove supercoils, can also move in the electrophoresis gel,

which is represented by special records and comet shaped stars. The intensities of these comet shaped images are interpreted in the form of frequency which can be detected in the DNA. In the following image, the larger comet length is showing the more damage to DNA.

Active ROS leads to more oxidation in DNA components, such as purine and pyrimidine. The oxidation of purine and pyrimidine takes place in the form 8-OH-Gua, 8-OH- **Gua** or 8-OH-Guo as oxidation factors in serum, urine or plasma. The more the occurrence of these factors in serum the more is the DNA damage.

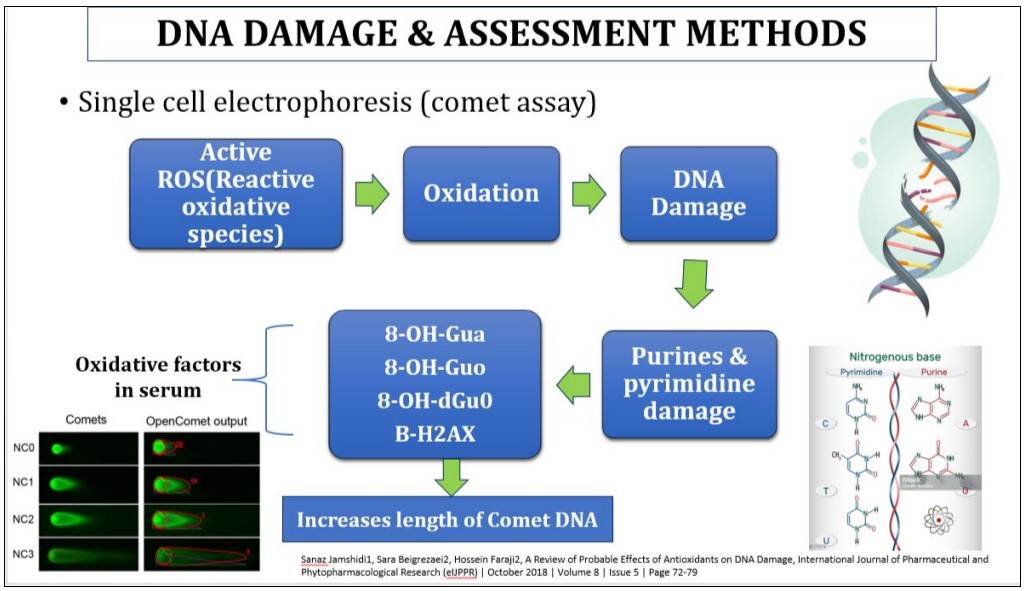


Figure 3: Schematic representation of correlation of DNA damage assessment tools.

Relation of OXIDATIVE STRESS AND AGING[25]

The elevated Reactive Oxygen Species causes decline in ATP Production thereby causes reduction in the Antioxidant defence mechanism, this causes damage to the cell, cell organelle, DNA, Lipids, Proteins causing Lipid Peroxidation leading to Proteolysis and Cease of cell division known as CELLULAR SENESCENCE affecting into Cell Death resulting in increased Rate of Aging.

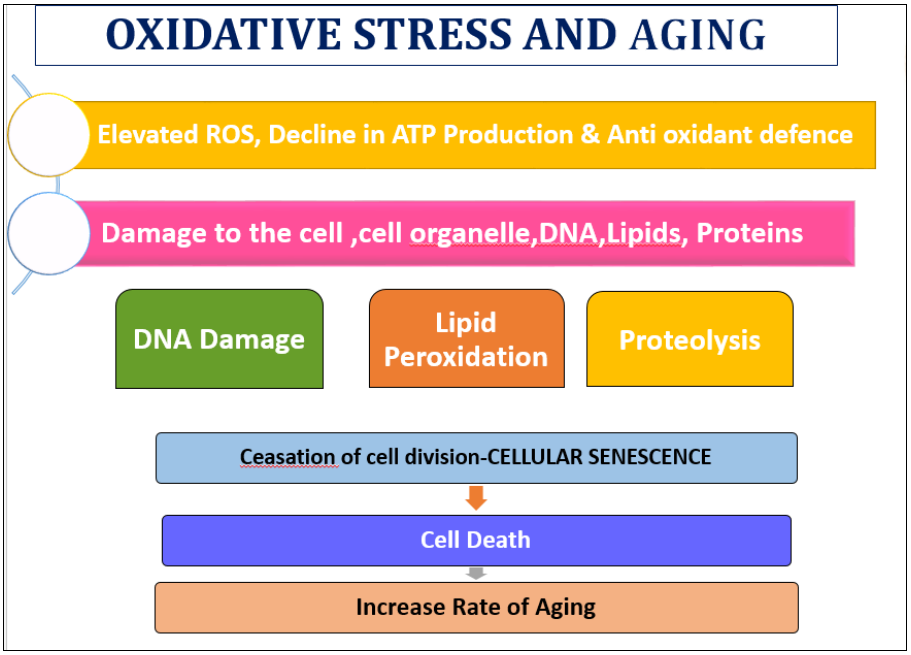
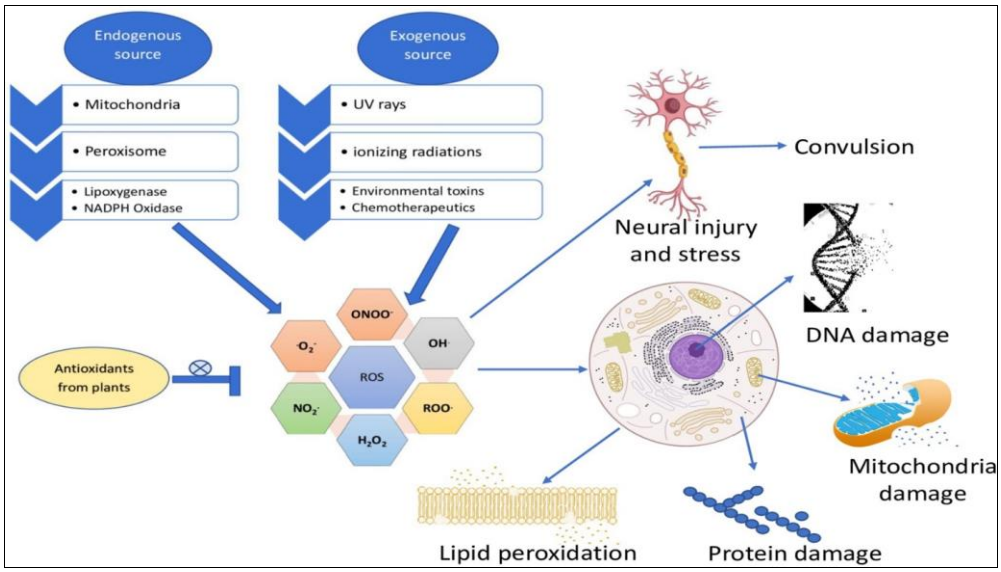


Figure 4: Schematic representation of correlation between oxidative stress and Aging.

Oxidative stress[26] can modify proteins, affecting their structure and function. This can lead to the accumulation of damaged proteins, which is a hallmark of aging This damage lipids in cell membranes, leading to loss of membrane integrity and cell death. This contributes to the aging process and the decline in tissue function.

DNA DAMAGE & ASSESSMENT METHODS[24,27,28,29] like Single cell electrophoresis (comet assay) illustrates the DNA damage and this DNA damage leads to mutation, malfunctioning of cells, contributing to aging and age related diseases like cancer, etc.**:**

Overall effect of free radicles and oxidative stress on various organs of human body[21]



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POSSIBLE MECHANISM OF ACTION OF RASAYAN DRAVYAS

1). Neutraceutical action / nutrient supporters

Many sources are referred to as antioxidant. Fruits and vegetables are known as the main source of antioxidants that are found in people's daily diet. Antioxidant compounds have a large variety generally including some vitamins such as C and E vitamins, beta carotene and polyphenols.

a. Effect of vitamin C on DNA damage[24]

Vitamin C (ascorbic acid) is known as one of the water soluble vitamins. Studies suggest that vitamin C have an important role in preventing the destruction of DNA i.e. it has the greatest effect in reducing the DNA damage which is observed in various studies in the people exposed to inappropriate diet, environmental pollutions and ionizing radiation.

Vitamin C also reduces amount of 8-OH-Gua, 8-OH- **Gua** or 8-OH-Guo which causes reduction in the comet length of DNA.

Effect of beta-carotene preventative of DNA damage

Beta carotene shows the protective effect against DNA damage due to the presence of antioxidants and polyphenols. Eg. Shigru, carrots.

b. Effect of selenium[30,31]

A study showed, the effect of selenium in reducing the DNA damage in leukocyte cell.

c. Effect of zinc[32,33]

Zinc results in reduction in DNA strands breaks. Zinc deficiency causes oxidative DNA damage and chromosome breaks have been reported in animals fed a zinc-deficient diet as per a study.

Eg. Guduchi[34]

d. Effects of polyphenols[35]

Reduction in DNA strands breaks and reduction in 8-OH-Gua level.

Eg. *Amalaki, Yashtimadhu*

2) Digestion promoter

Rasayana increases the digestive fire and helps also for absorption of food as well as well absorption of Rasayana dravyas in the body. Charaka in sutrasthan[36] has mentioned Deepaniya Mahakashay, in which Rasayana drugs like Pippali and Bhallataka has been included.

Mode of Action of Deepana dravyas

1. Stimulation of Vagus nerve.
2. Stimulation of glossopharyngeal nerve.
3. Stimulation of fundus and pylorus.

Mode of Action of Paachana Dravyas

1. Stimulation of the Vagus nerve which in turn secretes gastric juice.
2. Stimulates duodenum which leads to the secretion of digestive enzymes & hormones.
3. Stimulates the liver to secrete bile.
4. Stimulates pancreas to secrete pancreatic juice

बुद्धिप्रसादं बलमिन्द्रियाणां धातुस्थिरत्वं ज्वलनस्य दीप्तिम्।[37]

चिराच्च पाकं वयसः करोति संशोधनं सम्यगुपास्य- मानम् ॥ ६० ॥ अ.हृ.सु.18/60

3) Anti-inflammatory action[38,39,40]

Inflammation is the part of body's immune system. Inflammation is either acute or chronic inflammation. Cyclooxygenase (COX) is the key enzymes involved in the synthesis of prostaglandins, prostacyclins and thromboxanes which are convoluted in inflammation, pain and platelet aggregation. Steroidal and non-steroidal anti-inflammatory drugs (SAIDs and NASIDs, respectively) are currently the most widely used drugs for treating the acute inflammatory disorders, despite their renal and gastric negative secondary side effects. These drugs block COX-1 and COX-2 enzyme activity and COX enzymes contributes to the prostaglandin production. Long term uses of such drugs cause several adverse effects and damage various organs such as liver, gastrointestinal tract, etc leading to gastric lesions, cardiovascular, renal failure and gastrointestinal damage.

Glycosides from (Ashwagandha -Withaferin A), Tinosporide, a Phenolic compound from Guduchi, Gallic acid- from Triphala, Piperine an Alkaloid – Pippali, Berberine a Flavonoid, from Daruharidra, Quercetin and Kaempferol from Amalaki, Guduchi are the phytoconstituents that reduces the inflammation in the following pathways-

1. Inhibition of inflammatory mediators (e.g. TNF-a, IL-1B, IL-6)
2. Modulation of inflammatory enzymes (e.g. COX-2, LOX)
3. Suppressing NF-kB activation

These phtyoconstituents produces anti-inflammatory effects by showing inhibitory action on overexpression of pro-inflammatory modulators like tumour necrosis factor – alpha (TNF-α), prostaglandin (PGE2) synthesis and also inhibit cyclooxygenase-2 (COX-2) and nitric oxide production by inhibiting nitric oxide synthase (iNOS).

They also inhibit the inflammation caused due to the release of reactive oxygen species (ROS), interleukins (IL-8 & 1β) and nuclear factor κ light chain enhancer of activated B cells (NFκB) leading to arthritis and rheumatism.

4). Nootropic action/*Medhya*[41]

Medhya rasayanas are mentioned in *Charak Samhita, chikistasthana* which includes – *Guduchi, Mandukparni, Yashtimadhu and Shankhapushpi* and their medhya effect is explained.

1) *Mandukparni*

Mandukparni acts as neuroprotective, as it promotes brain development it has antioxidant like polyphenols and flavonoids. It also promotes the dendritic arborization and elongation dendritic arborization is the process by which neurons creates new dendritic trees and branches to form new synopses.[42]

2) Yashtimadhu (Glycyrrhiza glabra)[43]

'Glycyrrhizin' is a main component of yashtimadhu which is many times sweeter than sucrose. It provides the glucose bioavailability for brain and brain starts function properly. It also contains antioxidant like Flavonoids which causes free radical scavenging and it is also a good memory enhancer.

***3. Guduchi (Latin name- Tinospora cordifolia)*[44]**

Guduchi acts as **Anti-oxidant action and Immunomodulatory agent.**

- **Alkaloid (Palmatine) causes– Scavenging of free radicals and Inhibits lipid peroxidation and Enhances macrophage phagocytosis**
- Flavonoids (Quercetin) - Quenches singlet oxygen, Scavenges ROS and Stimulates T-caell proliferation.
- Phenolic acids (Gallic acid) - Inhibits hydroxyl radical formation and Activates NF-κB pathway
- Terpenoids (Ursolic acid) - Enhances antioxidant enzyme activity and Inhibits hydroxyl radical formation

These phytoconstituents also stimulates the release of neuromodulators and neuronal dendritic growth and Zinc and copper in *Guduchi* acts as Antioxidant and helps in maintaining the Hippocampal neurons and thereby acts as Memory enhancers.[45]

5) Cellular regeneration

Ayurveda has described the formation of basic components of our body as *Dhatus* and also elaborated the formation *Dhatus* in a sequential manner such as *Rasa to Rakta*, to *Mansa* and likewise all *Sapta dhatus* are formed. This is known as *Dhatu Utpatti Karma*. So formation of excellence in *Dhatu* formation *Ahara Rasa* is required which must have all the required nutrional values for the nourishment of *Sapta Dhatus* and also *Dhatwagni*.

Modern perspective the nutrients from the food, gets absorbed through digestive system which lately forms plasma, blood, muscles etc.

On the basis of classical text here trying to correlate the *Dhatu* formation by modern physiology

After digestion

•Nutrients, electrolytes, glucose, proteins, minerals, Fe, B12, Folic acid

↓

Plasma

↓

Entered into Liver cells

(Liver stores Fe, and process amino acids, glucose, Vit B12,)

↓

Ranjak pitta (heme oxygenase) in the liver and spleen

Mitochondria provides energy

(i.e. Dhatwagni)

Helps convert these nutrients into RBC in bone marrow

RBC undergoes further maturation and expelling the nucleus to fully matured RBC

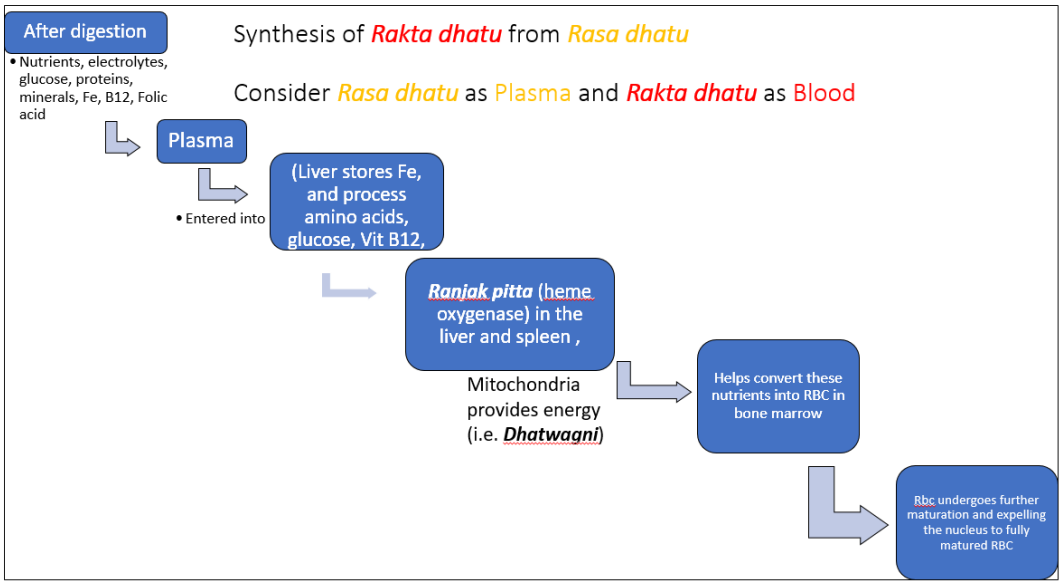

Figure 5: Schematic representation of formation of Rakta dhatu or blood cells from Ahara rasa.

Here after digestion Nutrients like electrolytes, glucose, proteins, minerals, Fe, B12, Folic acid get absorbed from digestive system and entered into plasma. This plasma again entered into liver where the liver procecced on them. Liver metabolized porphyrins which is pigment give color to RBC. Here we can correlate Porphyrins with ranjak pitta. Lately, RBC get formed in bone marrow and then expels the nucleus to fully matured RBC.

6) Rejuvination

Aging is a complex, irretrievable, dynamic process that involves a number of factors and its subject to number of environmental and genetic influences. Aging is collective term used for the complex detrimental physiological changes that reduce the functional ability of cell. Oxidative stress, telomerase shortening, inflammation regulates the aging process.

In Charaka sutrasthan, shadverachanshtashritiya adyaya, chapter 4, Vayasthapana mahakashaya has been mentioned.[46]

वय स्थापन गण - अमृताऽभयाधात्रीमुक्ताश्वेताजीवन्त्यतिरसामण्डूकपर्णीस्थिरापुनर्नवा इति दशेमानि वयःस्थापनानि भवन्ति (५०) (च.सू.४/१८)

Some examples are given below[22]

1) **mandukparni centella** asiatica increases the telemerase activity and it's an antioxidant by this it does the function of rejuvenation.
2) **Guduchi tinospora** cordifolia increases the viability and repair the dna damage
3) **Aamalaki** is an antioxidant and its decreases the free radicles by which it protects the body from cell death.

7). Cardioprotective effect of Rasayana dravyas[47,48]

Rasayana drugs have a great effect on cardiovascular system. Some drugs act as a protective action and some does the repairing actions.

Protective action

Chemical component Vit C, Berberin, gallic acid which is found in drugs like *Amalaki, Haritaki Guduchi* shows anti-inflammatory and anti-oxidant effects by reducing oxidative stress and inflammation of cardiac muscles.

Flavanoids like Querentin, Kaempferol which is found in drugs like *Guduchi*, *Ashwagandha*, *Amalaki*, etc regulates the blood pressure and helps to vasodilation.

Terpenoids which is majorly present in *Guduchi* helps to modify the lipid profile by decreasing the triglycerides and LDL cholesterol and also it prevents the plaque formation, so its shows anti atherosclerotic effects.

Repairing actions

When there is physiological or pathological cell or tissues damage or inflammation of heart and blood vessels taken place, then diagnostic markers are released into blood serum. Diagnostic markers for the cardiovascular system helps to identify conditions related to the heart and blood vessels.

Some examples of diagnostic markers like- Troponin- indicates myocardial infarction (heart attack) or cardiac damage.

Cardiac enzymes like AST (Asperate aminotransferase), ALT (Alanine transaminase) LDH (Lactate dehydrogenase) may indicate cardiac damage or infarction.

There are some drugs that repairs the damage of cardiac tissues that leads to prevent the elevation of cardiac markers.

Some examples are

1) Karveer (Nerium olender)
2) Arjuna (Terminalia arjuna)
3) Mandukparni (Centella asiatica)

7) Nephroprotective effect of Rasayana dravyas[48]

Due to pathological condition, when renal blood flow decreases, there is decreasing in GFR due to decreased net ultrafiltration pressure which leads to ischemic injury. This resulting in oxygen partial pressure which produces ROS (Reactive oxidative species) produces which further leads to cell death(apoptosis) resulting in kidney damage.

Rasayan drugs like *Guduchi* and *Ashwagandha* which has Flavanoids, quercetin like components down regulates the TNF-α, IL-1β, IL-6, COX-2 that inhibit the ROS formation in kidneys.

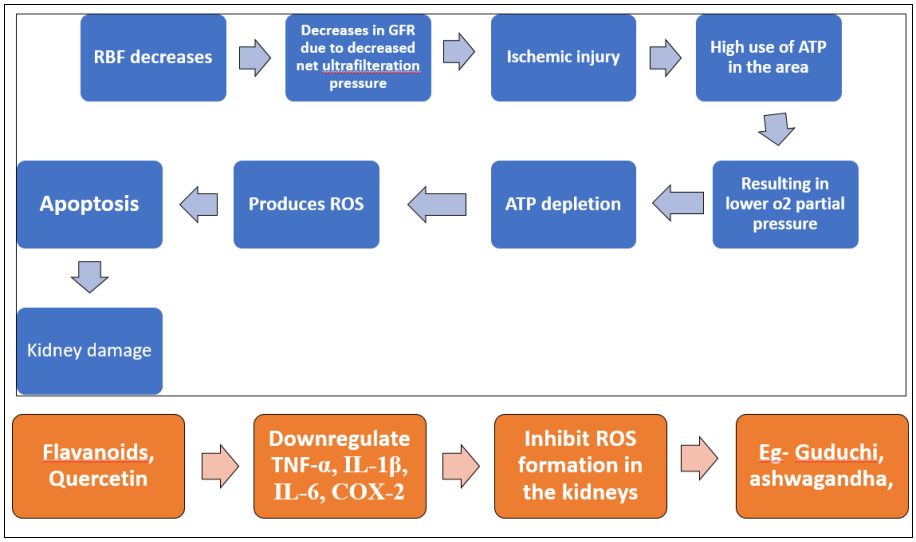

Figure 6: Schematic representation of formation of Nephroprotective action of some ayurvedic drugs.

9) Detoxification (Shodhana)[49, 50]

The liver detoxifies the body physiologically, but due to some pathological factors this process may get obstructed. So there are some drugs that promotes the action of liver.

Citrus species- Significantly raised the level of antioxidant enzymes- superoxide dismutase and catalase.

Clitoria ternatea- Normalized the levels of total and direct bilirubin.

Coriandum sativum- Significant reduction in the values of SGOT, SGPT, SALP, LPO, total bilirubin

Cyperus rotundus- Increase in the cell HepG2 cell viability –indicating restoration of the liver architecture toward normal.

Shodhan- As a treatment purpose *Shodhana chikitsa* is one of the important method to cure the diseases. Some *Rasayana* drugs has been used for *shodhana* karma.

Drugs like Haritaki, Guggul and Vacha Are the drugs used for shodhan karma.

These drugs has properties[51] of Katu, tikta, kashay rasas, Vishad, laghu, ruksha guna, Ushnavirya and Katuvipaka. Due to such properties it does the aampachana and clean the channels by detoxifying metabolic waste the further activates the microcirculation and improve tissue perforation.

DISCUSSION

Rasayana is a unique concept described in *Ayurveda* which is responsible for rasa - ayan i.e. Rasadi dhatu formation and thereby rejuvenation and cell regeneration which is the prime factor in survival and dhatu restoration. Various factors are responsible that causes halt in the cell regeneration processes by many different pathways which the causative factors are leading to cell apoptosis, cell degeneration and this leads to ageing. *Rasayan dravyas* acts by acting on various different pathways to restore the *dhatu* restoration, cell regeneration and thereby repair tissue damage and check cell apoptosis. These *Rasayan dravyas* acts in various mechanisms such as Immunomodulatory Action, Adaptogenic Action, Nootropic Action, Digestion Promoter, Cellular Regeneration/Dhatu-Poshan, Antiinflammatory Action, Rejuvination/*Jara Rasayan*, Nephroprotective Action, Cardioprotective Action, etc. each drug have their unique phytochemical constituents, the *dravyas* show their action accordingly and

causes cell regeneration and repairing cell damage, which is the main action of *Rasayan dravyas*.

CONCLUSION

Rasayana dravyas have broad spectrum activities as they possess different phytochemical constituents and different *Rasapanchakas*, thereby these *Rasayan dravyas* causes rejuvenation and delays ageing as by different pathways and causes cell restoration or restores cells damage, thereby delaying the degenerative phase i.e. ageing. So, it can be concluded that *Rasayan dravya* delineated in Ayurveda plays a crucial role in preventing or delay age related factors or diseases but the mode of action has still to be explored with the help of in vivo studies and clinical studies.

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