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Review Article

FREE RADICAL MEDIATED DISEASES AND THEIR PREVENTION : AN AYURVEDIC PERSPECTIVE

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ABSTRACT

Free radical production occurs continuously in all cells as part of normal cellular function. However, excess free radical production originating from endogenous or exogenous sources might play a role in many diseases. Antioxidants prevent free radical induced tissue damage by preventing the formation of radicals, scavenging them, or by promoting their decomposition. The disease preventive and health promotive approach of '*Ayurveda*', which takes into consideration the whole body, mind and spirit while dealing with the maintenance of health, promotion of health and treating ailments is holistic and finds increasing acceptability in many regions of the world. Ancient *Ayurvedic* physicians had developed certain dietary and therapeutic measures to arrest/delay ageing and rejuvenating whole functional dynamics of the body system. This revitalization and rejuvenation is known as the *'Rasayan chikitsa'* (rejuvenation therapy). *Rasayana* is intended in classical *Ayurveda* as an effective tool to synthesize the excellent quality of *Dhatu* that entails the prevention and alleviation of senility and diseases. Experimental studies done on various *Rasayana* drugs prove that they have immune stimulant, antioxidant, adaptogenic and anti-stress properties. *Rasayana* drugs consist of the substances which are rich in Vitamin C, Vitamin E, Beta carotene, riboflavin. So these substances are capable of counteracting the damaging effect of oxidation by working as anti-oxidants & prevent aging process. Over about 100 disorders like rheumatoid arthritis, hemorrhagic shock, CVS disorders, cystic fibrosis, metabolic disorders, neurodegenerative diseases, gastrointestinal ulcerogenesis and AIDS have been reported as reactive oxygen species mediated. In this review, the role of free radicals in these diseases has been briefly reviewed. '*Rasayana*' plants with potent antioxidant activity have been reviewed for their traditional uses, and mechanism of antioxidant action.

KEYWORDS: Free radicals, Free radical mediated disease, Antioxidants, *Rasayana.*

INTRODUCTION

Ayurveda science is the life science having two aims, one is to maintenance of health of healthy person and the second is to cure diseases of diseased person[1]. The current modern definition of health is "Health is a state of complete physical, mental and social well being and not merely absence of disease. (W.H.O.) which is already mentioned by Sushrut[2]. In present era, free radical mediated diseases are expanding like anything. In recent years, a substantial body of evidence has developed supporting a key role for free radicals in many fundamental cellular reactions and suggesting that oxidative stress might be important in the pathophysiology of common diseases including atherosclerosis, chronic renal failure, and diabetes mellitus. Prevention might be the right choice against such kind of diseases. In *Ayurvedic* classics plenty of *Rasayanas* are explained for longevity as well as management of diseases. The branch of *Rasayana* or rejuvenation is one of the eight specialized branches of *Ayurveda* that primarily deals with the maintenance of health. *Rasayan chikitsa* consist of certain dietary & therapeutic measures like herbal preparations which are able to correct as well as improve *Dhatus* immunity by a proper nutrition. The aim of this review is to consider mechanisms of free radical formation in the body, the consequences of free radical induced tissue damage, and the function of antioxidant defence systems in health and disease.

AIM AND OBJECTIVES

1. To evaluate role of free radicals in pathology of disease.
2. To evaluate the function of antioxidant defence system against free radical mediated diseases.
3. To evaluate the role of *'Rasayana chikitsa'* in the management of Free radical mediated diseases.

MATERIALS AND METHODS

Ayurvedic textual materials were referred, mainly *Charaka samhita, Sushruta samhita, Astanga hridaya* and available commentaries of these *Samhitas,* for the study. Some modern books of biochemistry, journals etc. have also been looked over. From these books references have been collected and studied systematically.

DISCUSSION

Concept of free radicals

Free radicals are atoms, ions or molecules that contain an unpaired electron. Thus, they become electrically charged because number of negatively charged electron does not match with positively charged protons. When a molecule looses or gains a single electron in its outer orbit, it becomes free radical. In fact a free radical is defined as "A molecule that can exist independently for a period of time with one or more unpaired electrons." Free radicals are unstable chemicals formed in the body during normal metabolism or exposure to environmental toxins

such as air, food and water pollution. Free radical helps our body to generate energy and fight infection but when we have too many free radicals they attack healthy cells causing them to age prematurely. These free radicals and other reactive oxygen species such as Super oxides, hydrogen peroxide and hydroxyl radicals are molecular species capable of independent existence that contain an unpaired electron in an atomic orbital. Some of the important free radicals generated in our body are – superoxide radical, hydroxyl radical, & nitric oxide radical. The Hydroxyl radical is extremely toxic but short lived. The sources of these reactive species are – xanthine oxides, which generates super oxides (e.g. during reperfusion injury of ischaemic organs), cycloxygenase and lipoxygenase in the sytosol, which produce hydroxyl and peroxyl radicals. Stimulated Neutrophils produce superoxides, cytochrome oxidase system located in mitochondria produce superoxide radicals during metabolism. Other sources of Free radicals in the body are lysosomes and peroxisomes nuclear endoplasmic reticulum, plasma membrane and all phagocytic cells. Thus, under normal conditions, free radicals are continuously produced as intermediates in cellular metabolism. The exogenous sources of F.R.'s include oxidant toxins (e.g. Doxorubicin), Drug oxidations (e.g. paracetamol), Ionizing radiations, Environmental pollution, cigarette smoke and sunlight. They are unstable chemical formed in the body and can cause degenerative changes and other diseases like cancer, myocardial infarction etc. [3]

Radical formation in the body occurs by several mechanisms, involving both endogenous and environmental factors (fig 1).

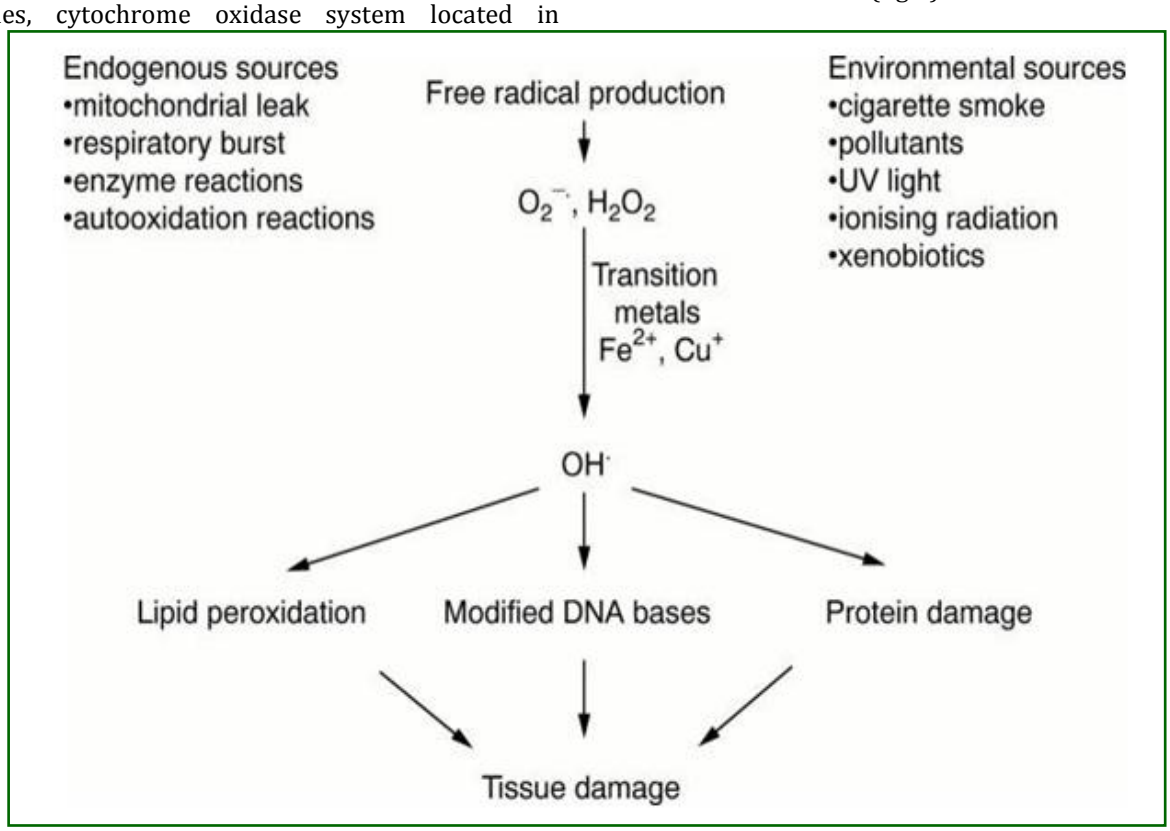

Figure 1: Major sources of free radicals in the body and the consequences of free radical damage

As these molecules are generated within these cells and are highly reactive, therefore they act in situ i.e., very close to the site where, they are generated and most structures in the vicinity are vulnerable. Free radicals attack double bonds in polyunsaturated lipids within cell membrance causing lipid peroxidation. This leads to irreversible loss of fluidity and structural integrity of the membrane, resulting in loss of membrane functions and ultimately, cell death. Degradation products can damage nucleic acids, leading to mutagenesis and carcinogenesis.

They cause oxidation of vital enzymes, leading to dysfunction, inactivation and damage to structural proteins like collagen and Elastin. Oxidised proteins are accumulated in ageing.

Free radicals cause depolymerization of poly saccharides like hyaluronidase leading to structural and funcational dysfunctions. Damage to carbohydrate moity of cellular receptors produce loss of cell functions.

Free radicals also include DNA strand break and base modification. Thus individual bases of DNA strands can be altered leading to mutagenesis and carcinogenesis.

Free radical oxidative damage has been found to be increased in patients with a variety of diseases and natural antioxidant defences have been found to be defective in many of the same diseases. Free radicals released by disease process, infections, trauma, toxins etc. may be secondary factors in perpetuation of diseases. Some of the diseases where free radicals play a significant role, either directly or indirectly are Rheumatoid Arthritis, inflammatory gut disorder like ulcerative colitis, connective tissue diseases, atherosclerosis, reperfusion injury diseases like Myocardial infarction, cerebral ischaemia and stroke, Intestinal ischaemia, Acute Renal

necroises, cancer, parkinsonism, Alzheimers dementia, diabetes mellitus and Ageing process.

Role of free radicals in pathology of disease

Cancer

Permanent modification of genetic material resulting from "oxidative damage" incidents represents the first step involved in mutagenesis, carcinogenesis, and ageing. DNA mutation is a critical step in carcinogenesis and elevated levels of oxidative DNA lesions have been noted in various tumours, strongly implicating such damage in the etiology of cancer. ROS-induced DNA damage involves single or double-stranded DNA breaks, purine, pyrimidine, or deoxyribose modifications, and DNA cross-links. DNA damage can result in either arrest or induction of transcription, induction of signal transduction pathways, replication errors, and genomic instability, all of which are associated with carcinogenesis. DNA damage, mutations, and altered gene expression are thus all key players in the process of carcinogenesis.[4] The involvement of oxidants appears to be the common denominator to all these events.

Cardivascular disease

The ROS-induced oxidative stress in cardiac and vascular myocytes has been linked with cardiovascular tissue injury.[5] Regardless of the direct evidence for a link between oxidative stress and cardiovascular disease, ROS-induced oxidative stress plays a role in various cardiovascular diseases such as atherosclerosis, ischemic heart disease, hypertension, cardiomyopathies, cardiac hypertrophy and congestive heart failure. [6]

The major sources of oxidative stress in cardiovascular system involve:

(i) The enzymes xanthine oxidoreductase (XOR),
(ii) NAD(P)H oxidase (multisubunit membrane complexes) and
(iii) NOS as well as
(iv) The mitochondrial cytochromes and
(v) Haemoglobin. [7]

Oxidative stress is associated with increased formation of ROS that modifies phospholipids and proteins leading to peroxidation and oxidation of thiol groups.[8] The assaults by ROS lead to changes in membrane permeability, membrane lipid bilayer disruption and functional modification of various cellular proteins. In addition to cellular protein and lipid damage, abnormalities in myocyte function due to increased oxidative stress are considered to be associated with the effects of ROS on subcellular organelles.

Rheumatoid arthritis

Rheumatoid arthritis is an autoimmune disease that causes chronic inflammation of the joints and tissue around the joints with infiltration of macrophages and activated T cells.[9] The pathogenesis of this disease is linked predominantly with the formation of free radicals at the site of inflammation. Oxidative injury and inflammatory status in various rheumatic diseases was confirmed by increased levels of isoprostanes and prostaglandins in serum and synovial fluid compare to controls. Oxidative conditions in synovial tissue are also associated with a higher incidence of p53 mutations.[10] T cells isolated from the synovial fluid of patients with rheumatoid arthritis show signs of decreased intracellular GSH level, impaired phosphorylation of the adaptor protein linker for T-cell activation (LAT) and the "primed" CD45RO phenotype.[11] The migration of monocytes and lymphocytes into the rheumatoid arthritis synovium is mediated by the abnormal expression of several adhesion molecules (ELAM-1, VCAM-1, ICAM-1, ICAM-2) ; this can be explained by the abnormal induction of redox-sensitive signaling pathways.

Diabetes

There is increasing evidence that free radical induced damage also plays a significant part in the development of insulin resistance, β-cell dysfunction, impaired glucose tolerance, and type 2 diabetes mellitus. Hyperglycemia can induce oxidative stress, which increases with age, via several mechanisms including glucose auto oxidation, the formation of advanced glycation end-products (AGE). Other circulating factors that are elevated in diabetics such as free fatty acids and leptin also contribute to increased ROS. There is a significant increase in protein glycation (AGE) with age, which is also increased in diabetics. The accumulation of AGE leads to an increase in the micro vascular lesions, which are present in diabetic retinopathy, and is also responsible for cardiovascular complications, which are seen in diabetic patients.[12] The damage caused by ROS has also been implicated in primary open angle glaucoma (POGA), which is the leading cause of irreversible blindness and the second most common cause of all blindness after cataracts. The incidence of POAG is linked to old age, thus advanced age represents a major risk factor for this disease.

Neurological disorders

The brain is particularly vulnerable to oxidative damage because of its high oxygen utilisation, its high content of oxidisable polyunsaturated fatty acids, and the presence of redoxactive metals (Cu, Fe). Oxidative stress increases with age and therefore it can be considered as an important causative factor in several neurodegenerative diseases, typical for older individuals.[4]

Alzheimer's disease

The brains of patients with Alzheimer's disease (AD) show a significant extent of oxidative damage associated with a marked accumulation of amyloid- α peptide (Aα), the main constituent of senile plaques in brain, as well as deposition of neurofibrillary tangles and neurophil threads. The direct evidence supporting increased oxidative stress in AD brain include (i) increased Cu, Fe, Al, and Hg content; (ii) increased lipid peroxidation and decreased polyunsaturated fatty acid content, and an increase in 4-hydroxynonenal, an aldehyde product of lipid peroxidation in AD ventricular fluid; (iii) increased protein and DNA oxidation; (iv) diminished energy metabolism and decreased cytochrome c oxidase content; (v) advanced glycation end products (AGE), malondialdehyde, carbonyls, peroxynitrite, heme oxygenase- 1, and SOD-1 in neurofibrillary tangles, (vi) the presence in activated microglia surrounding most senile plaques of

nitrotyrosine, formed from peroxynitrite (ONOO•α). As mentioned above, elevated production of Aα, as a preventive antioxidant for brain lipoproteins under the action of increased oxidative stress and neurotoxicity in ageing, is postulated to represent a major event in the development of Alzheimer's disease.[13]

Parkinson's disease

Parkinson's disease (PD) involves a selective loss of neurons in an area of the midbrain called the substantia nigra.[14] The cells of the substantia nigra use dopamine (a neurotransmitter-chemical messenger between brain and nerve cells) to communicate with the cells in another region of the brain called the stratium. Thus, a reduction in nigral dopamine levels results in a decrease in stratial dopamine that is believed to cause PD symptoms.[15] A majority of studies explored the effect of oxidative stress that contributes to the cascade of events leading to dopamine cell degeneration in PD. The occurrence of oxidative stress in PD is supported by both postmortem studies and by studies demonstrating the capacity of oxidative stress to induce nigral cell degeneration. There is evidence that there are high levels of basal oxidative stress in the substantia nigra pars compacta (SNc) in the normal brain, but that this increases in PD patients. However, other factors involving inflammation, excitotoxic mechanisms, toxic action of nitric oxide, and mitochondrial dysfunction play roles in the etiology of PD.

Stroke

In Western countries stroke is the main cause of disability and mortality among the aging population, and ischemic stroke accounts for about 75% of all cases while hemorrhagic stroke is responsible for almost 15% of all strokes. There is evidence that stroke is associated with free radicals arising from sources such as xanthine oxidase, cyclooxygenase, inflammatory cells and mitochondria, and these can potentially cause neuronal death. The mitochondrial electron transport chain is altered during ischemia and reperfusion and is also a likely source of free radicals. The accumulation of blood borne inflammatory cells such as neutrophils and monocytes/macrophages, which can occur during reperfusion, can also promote further oxidative stress. Increased levels of oxidative damage to DNA and evidence for lipid peroxidation has also been demonstrated in ischemic stroke patients.

Huntington's disease (HD)

This is an inherited, autosomal dominant neurodegenerative disease, which causes uncontrollable movements and restlessness as well as irritability and depression.

Direct evidence for a defect in oxidative phosphorylation in HD patients is supported by the discovery of a threefold increase in lactate concentrations in the occipital cortex and in the basal ganglia. There is further evidence to support the involvement of free radicals in the pathogenesis of HD in that increased levels of F_2-isoprostanes have been detected in the cerebro-spinal fluid of HD patients compared to the control group.

Neonatal Oxygen Radical Diseases

The preterm baby may be specially vulnerable to "free" oxygen radicals, because it is exposed more liberally to oxygen radical generation and its defence against oxygen radicals is low. It has, therefore, been postulated that a "neonatal oxygen radical disease" does exist. Diseases like:

- Bronchopulmonary dysplasia
- Retinopathy of prematurity etc

Defence Mechanism to Free Radicals-Anti-oxidants

Antioxidants can be broadly defined as any substance that when present at low concentrations compared to those of an oxidizable substrate significantly prevent or delays any oxidation of that substrate. Human body has its own antioxidance defences to protect against hazardous effects of oxidative stress given by free radicals. The major ones are intracellular and extracellular antioxidants.

Intracellular antioxidant include enzymes like

1. Manganese containing superoxide Dismutase (SOD)
2. Catalase
3. Selenium containing Glutathione peroxidase (GSH)
4. Glutathione reductase

Extracellular antioxidants include

1. Transferrin & Lactoferrin (Iron binding proteins)
2. Ceruloplasmin (copper containing enzyme)
3. Albumin & Haptoglobin – Haemopexin Complex, which prevent the chances of lipid peroxidation.

Mechanism of action

Two principle mechanisms of action have been proposed for antioxidants.[16]

1. The first is a chain- breaking mechanism by which the primary antioxidant donates an electron to the free radical present in the systems.
2. The second mechanism involves removal of ROS/reactive nitrogen species initiators (secondary antioxidants) by quenching chain-initiating catalyst.

Antioxidants may exert their effect on biological systems by different mechanisms including electron donation, metal ion chelation, co-antioxidants, or by gene expression regulation.[17]

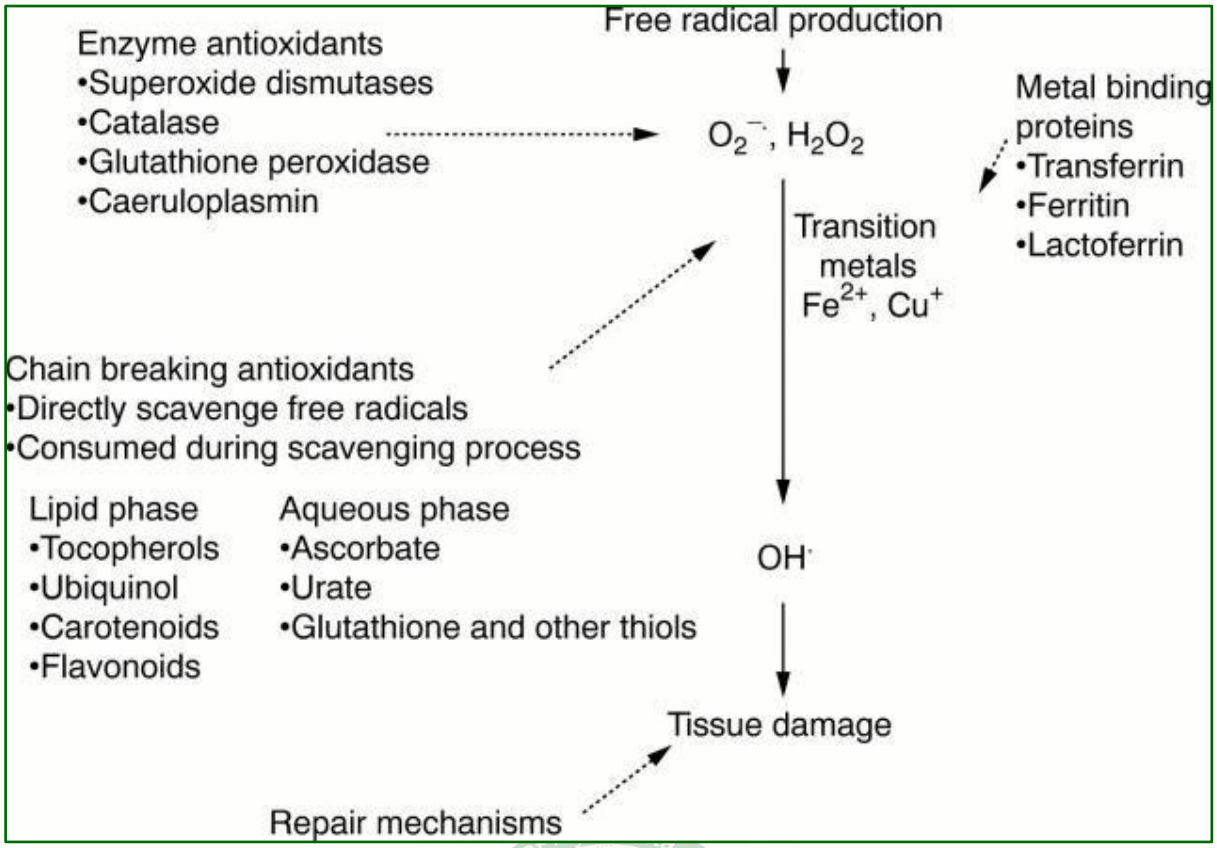

Figure 2: Antioxidant defense system against free radical damage

Levels of antioxidant action

The antioxidants acting in the defense systems act at different levels such as:

1. Preventive
2. Radical scavenging
3. Repair and de novo
4. Adaptation

1. The first line of defense is the preventive antioxidants, which suppress the formation of free radicals. Glutathione peroxidase, glutathiones transferase, phospholipid hydroperoxide glutathione peroxidase (PHGPX), and peroxidase are known to decompose lipid hydroperoxides to corresponding alcohols. Glutathione peroxidase and catalase reduce hydrogen peroxide to water.
2. The second line of defense is the antioxidants that scavenge the active radicals to suppress chain initiation and/or break the chain propagation reactions.
3. Various endogenous radical-scavenging antioxidants are known: some are hydrophilic and others are lipophilic. Vitamin C, uric acid, bilirubin, albumin, and thiols are hydrophilic, radical-scavenging antioxidants, while vitamin E and ubiquinol are lipophilic radical-scavenging antioxidants. Vitamin E is accepted as the most potent radical-scavenging lipophilic antioxidant.
4. The third line of defense is the repair and de novo antioxidants. The proteolytic enzymes, proteinases, proteases, and peptidases, present in the cytosol and in the mitochondria of mammalian cells, recognize, degrade, and remove oxidatively modified proteins and prevent the accumulation of oxidized proteins.
5. The DNA repair systems also play an important role in the total defense system against oxidative damage. Various kinds of enzymes such as glycosylases and nucleases, which repair the damaged DNA, are known.
6. There is another important function called adaptation where the signal for the production and reactions of free radicals induces formation and transport of the appropriate antioxidant to the right site. [18]

Concept of *Rasayana*

Ancient Ayurvedic physicians had developed certain dietary and therapeutic measures to arrest/delay ageing and rejuvenating whole functional dynamics of the body system. This revitalization and rejuvenation is known as the *'Rasayan chikitsa'* (rejuvenation therapy).

- According to the Panchabhautic concept of Ayurveda, it reveals that predominance of *Prithvi* & *Apa mahabhut*[19] of the *Dravyas* provide *Sthairyata*, *Ghanata*, *Kledan, Snighnata, Apyayan & Sandhankar* (*Sanyogakar*) to the *Dhatus*. So work as *Vayasthapak* (prevents degeneration) [20] of *Dhatus* & work to improve quality of *Dhatus*.
- The most of the *Rasayan dravyas* are *Ushnavirya*. So because of predominance of *Teja Mahabhuta* they improve the metabolic activities of *Dhatwagnis* & improve quality of *Dhatu* by nourishing them.
- *Rasayana* drugs selectively enhance the activity of certain antioxidants, they reduce the oxidative damage of cells & prevent the degenerative changes of *Dhatus*.
- It is a specialized type of treatment which promote activities of basic fundamentals of body i.e., *Dosha*,

Dhatu, *Agni* & *Srotas*, which comprehensively results in good health. Basically acting on *Agni* they impart best qualities of *Dhatu. "Prashastam Ras-rudhiradinam yo labhopayab sa rasayanam"- Arundatta.*

- *Rasayan* drugs consist of the substances which are rich in Vitamin C, Vitamin E, Beta carotene, riboflavin. So these substances are capable of counteracting the damaging effect of oxidation. So they work as anti-oxidants.
- In *Amalaki* main constituents are Vitamin C, carotene, riboflavin. So it has role in cellular oxidation reduction.
- Withanolide in *Ashwagandha* increase levels of three natural antioxidants like super oxide, dismutase, Catalase, Glutathione peroxidase & helps to prevent damage of cells. So work to prevent aging process. *Vayahsthairyakaranam Labhopayo rasayanam- Sushrut.*

Mode of action of *Rasayana dravya*

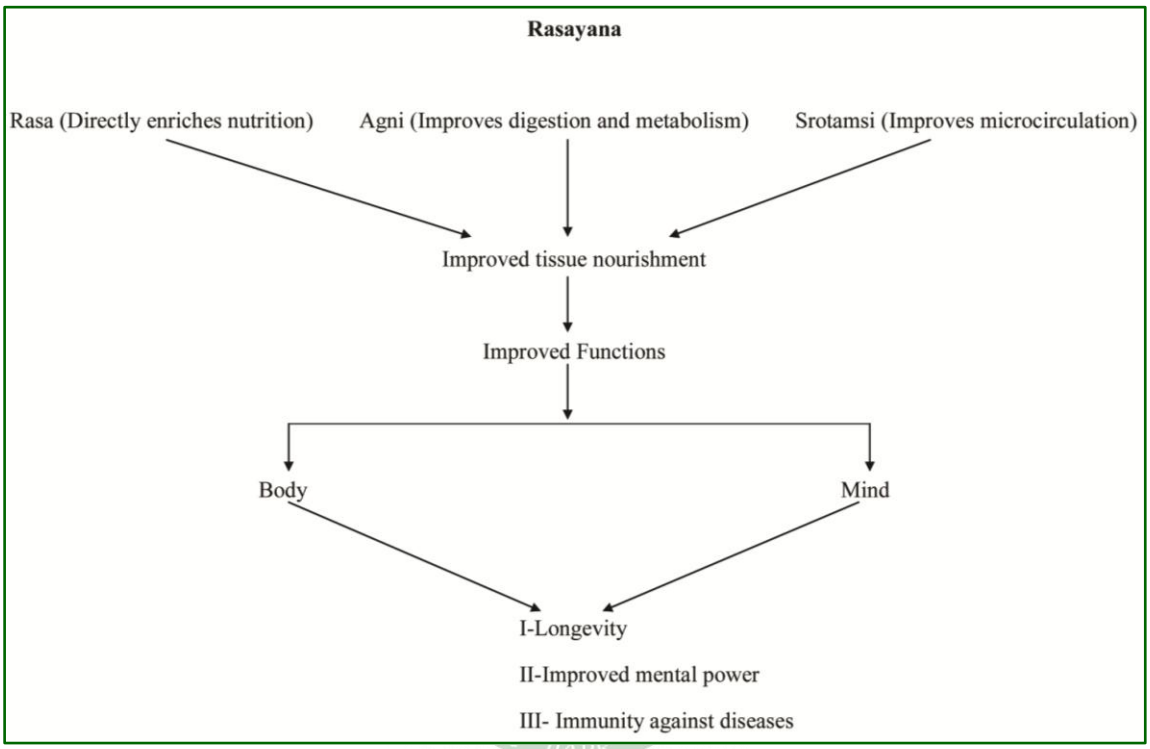

Figure 3: Mode of Action of *Rasayana Dravya* at different level

Rasayana drugs and measures act at one or all the three above mentioned levels. As a result rich, good and healthy tissues develop in the body.

1. Acting at all the level of rasa by directly enriching the nutritional value of the circulating plasma. Examples are *Draksa*, milk, *Satavari* and all such direct nutrients.
2. Acting at the level of Agni i.e. at the level of digestion and metabolism. This group of *Rasayana* improve the digestion, absorption and metabolism leading in turn to improved nutritional status. Examples are *Pippali*, *Haritaki, Citraka* etc.
3. Acting at the level of *Srotamsi* i.e. the microcirculatory channels carrying nutrition to the tissues. These *Rasayanas* clean and and activate the microcirculatory channels i.e. *Srotasuddhi* leading to improved micro-circulation and tissue perfusion. Examples are *Guggulu, Pippali, Rasona* etc.[21]

Researches in the Field of *Rasayan*

***Rasayan* in cancer**

Administration of *Rasayanas* was found to enhance the proliferation of spleen cells significantly especially in the presence of mitogen. A similar result was also seen with bone marrow cells. However mitogenic stimulation could not be observed. Esterase activity was found to be enhanced in bone marrow cells indicating increased maturation of cells of lymphoid linkage.[22] Oral administration of *Rasayan* significantly increased total WBC count, bone marrow cellularity, natural killer cell and antibody dependant cellular cytotoxicity in gamma radiation (4Gy) expose mice. *Rasayanas* reduced radiation induced perioxidation in liver.[23] *Rasayan avaleha* gave better results in controlling the adverse effect of chemo-therapy and radiotherapy such as nausea, vomiting, mucocitis, fatigue, xerostomia, alopecia.[24]

***Rasayan* in Tuberculosis**

Rasayan compound is beneficial in the management of tuberculosis with anti-Koch's treatment. It significantly decrease cough, fever, dyspnoea, haemoptysis, and increased body weight.[25]

***Rasayan* in Rheumatoid arthritis**

Vardhaman pippali rasayan is effective in the management of *Aamavata* (rheumatoid arthritis). A significant decrease in erythrocyte sedimentation rate was also noted.[26]

Rasayan in geriatrics

In senile memory impairment *Guduchyadi medhya rasayan* showed memory enhancement, antistress, antidepressant and anxiolytic properties.[27]

Rasayan in Genome stability

As per the studies on molecular correlates of genomic stability in rat brain cells following *Amalaki rasayan* therapy, the result convincingly indicate that, in control animals there was a distinct increase in DNA damage with age in neurons and astrocytes. But the animals treated with *Rasayan* showed significantly less DNA damage in brain cell demonstrating beneficial effect of *Rasayan* therapy towards maintenance in genomic stability. DNA damage may be proximal cause of aging.[28]

Rasayan in stem cell therapy

Regeneration of tissues after the disease condition like osteoarthritis, age related macular degeneration (AMD), Alzheimer's, injuries, trauma, heart attack, stroke, accident, or aging remains a challenge to modern medicine. Tissue specific *Rasayanas* could be tried for differentiation of stem cells and regenerate specific tissue of choice. *Rasayanas* known for their tissue specificity could also be tested in stem cells to reveal their differentiation inducing activity. In preliminary experimentation on *Medhya Rasayana*, there was a expression of nestin an early marker of neuronal stem cells differentiation when stem cells were treated with *Rasayana* extracts.[29] The vitamin C can regulate proliferation as well as differentiation of stem cells depending upon its concentration.[30] *Aamalaki* is rich source of vitamin C and may be acting through similar pathways. Ayurvedic preparations like *Rasayanas* could be explored for their role in potentiating stem cells for clinical applications.[31] *Piper longum* volatile oil extract improves the proliferation on mesenchymal stem cell.[32]

With the basic similarity in *Rasayana* drugs of Ayurveda and antioxidants of modern medicine, the effect of several Ayurvedic medicines have been investigated. Some of them are as follows:

1. *Manjistha (Rubia cordifolia)*
2. *Sigru (Moringa oleifera)*
3. *Bhallatak (Semecarpus anacardium)*
4. *Kapikacchu (Mucuna pruriens)*
5. *Brahmi (Bacopa monnieri)*
6. *Jatamamsi (Nardostachys jatamansi)*
7. *Yastimadhu (Glycyrrhiza Glabra)*
8. *Guduchi (Tinospora cordifolia)*
9. *Amlaki (Emblica officinalis)*
10. *Haritaki (Terminalia Chebula)*

CONCLUSION

Free radicals which are formed as intermediary byproduct of metabolism, have the tendency to damage various cells of the body. Free radical damage contributes to the etiology of many chronic health problems such as cardiovascular, inflammatory disease, diabetes, cancer etc. Antioxidants prevent free radical induced tissue damage by preventing the formation of radicals, scavenging them, or by promoting their decomposition. *Rasayana* therapy aids in reviving the health of a healthy person as well as in combating the disease of the diseased one. It enables the body to develop its own vital energy or the defensive mechanism against free radical related diseases. These act principally by strengthening the immune system of the body acting as both brain and body tonic. There is no doubt that antioxidants are necessary components for our health but we should not forget that the antioxidants and free radicals production should be in balance. Reducing externally free radical sources such as smoking, cigarettes, environmental pollutants, pesticides etc., in our life may be the better choice for eliminating hazardous effects of free radicals.

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