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ROLE OF FREE RADICALS AND ANTIOXIDANTS IN PHYSIOLOGICAL STRESS: AN AYURVEDIC VIEW

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ABSTRACT

Stress is an inevitable part of our current modern-day life-style it just cannot be eliminated totally. Stress is a situation which demand excess intake of oxygen which leads to the release of excess free radicals. Free radicals are found to be the root cause of all diseases. Similarly, ama (undigestable substances) formed as a part of impairment in the digestion is considered as the cause of all diseases. Agni(Digestive fire) impairment will occur at all levels, dhatwagn & bhootagni level all leads to the formation of ama. Also, every cell produces free radicals. Antioxidants are the substances that helps in neutralising the free radicals, so a powerful antioxidant system is essential. Rasayana chikitsa (rejuvenation therapy) is the rejuvenation therapy that arrest aging and rejuvenate whole functional dynamics of the body. This article is to analyse the role of free radicals and antioxidants in physiological stress with ayurvedic view.

Keywords: antioxidants, free radicals, rasayanam, stress

INTRODUCTION

Stress is a psychophysiological (mind and body) arousal that can fatigue body systems to the point of malfunction and disease [1]. Nowadays stress related diseases are being recognized as a new class of diseases that require different scientific requirement and medical evaluation. Failure of adaptation to stress may result in various diseases or even death and it can also increase the vulnerability of an organism to certain diseases. Vata being the main controller of mind and body contribute to the stress and stress related diseases. Free radicals are generated in the body at the time of energy production. At high concentrations, free radicals and radical derived reactive species are hazardous for living organism and damage all major cellular constituents (lipids, DNA, RNA and proteins). These free radicals are the root cause of many diseases. According to Ayurveda, agni is considered as the moola of health. Malfunctioning of agni leads to the production of Ama, which is responsible for the generation of all diseases. Human body possesses ability to combat against free radical damage by production of antioxidants. The excessive production of free radicals in the organism and the imbalance between the concentrations of these and antioxidants defences may be related to processes such as aging and several diseases among cancer, ischemic processes, senile dementia and diabetes are the main ones. Any disturbance in the removal of free radicals will cause accumulation of reactive oxygen species in the cells and will lead to harmful changes and disease. So, it is important to maintain the antioxidant defence system of cell in a healthy way.

STRESS

Stress, in general, is any situation or activity, which is not suited to a person's nature and is uncomfortable to him. As different people have different types of natures, one man's meat is another man's poison. According to oxford dictionary, stress is a state of affair involving demand on physical or mental energy. Autonomic nervous system and endocrine system are the two main systems that control stress arousal. Cortisol and aldosterone are the two main hormones that helps the body to cope up with stress.

Cortisol affects metabolism by increasing the availability of energy (in the form of glucose, fatty acids, and amino acids), either for the stress response or for recovery from an extreme period of over activity. It increases, as much as tenfold, a metabolic process of the liver called gluconeogenesis, through which the body forms glucose out of available glycogen and amino acids. Moreover, cortisol mobilizes both fatty acids and proteins in the blood. The mobilization of protein reduces the stores of protein in all body cells (except in the liver and in the gastrointestinal tract, which is where the mobilization takes place). Hence, if the stress response is maintained for a long period, the supply of protein available for the formation of mature white blood cells and antibodies diminishes to the point of disease susceptibility. In this way, prolonged stress can promote muscular wasting and impair the immune system.

When fatty acids are mobilized from adipose stores, they circulate through the bloodstream to be available as an energy source for muscle tissue. When fatty acids are used for physical resolution of the stress response, they present little health threat. However, high levels of fatty tissue in the blood appear to promote atherosclerosis (fatty plaquing of the arteries) especially when they are present over time.

Aldosterone is the other major adrenal cortex hormone secreted in increased amounts during the stress response. The body reacts to aldosterone by preparing itself for increased muscular activity and better dissipation of heat and waste products. It does this by retaining extra sodium (salt), which results in increased water retention. This leads to increases in blood volume, blood pressure, and the amount of blood the heart pumps out with each beat. As with other body systems, prolonged manifestation of the stress response can endanger the cardiovascular system.

Ayurveda defines health as a state of physical, mental and spiritual equilibrium of an individual. The total physiology of the body is contributed by tridoshas. As per tridosha theory, each cell of the human body functions normally when tridoshas are not vitiated. The vitiated doshas are responsible for all pathological changes in body and mind. When body or mind is exposed to stress of any type, both sareerika and manasika doshas along with other biological factors will take the necessary steps to face the situation. Since the Mana(mind) is mainly controlled by vata, which is also the controller of other doshas, vata dosha will have an important role in stress response.

FREE RADICALS AND ANTIOXIDANTS

A free radical is any species capable of independent existence that contains one or more unpaired electrons [2]. Chemically free radicals could be Oxygen, Carbon, Nitrogen or Vanadium centred molecules, but oxygen free radicals are mostly seen in aerobic organisms. Every cell is producing free radicals at the time of energy production through electron transport chain. They are the natural by products of chemical processes such as metabolism. Free radicals play a role in producing stress related changes at cellular level. Once free radicals are formed, a chain reaction can occur. The chain reaction may change the structure of lipid, making it more likely to become trapped in an artery. The damaged molecules may mutate and grow tumours. Or, the cascading damage may change DNA code. In general, free radical damage may involve any cellular content which include mitochondria, lysozymes, peroxisomes, nuclear endoplasmic reticulum and plasma membranes as well as sites within the cytosol.

Although the free radicals are produced daily they are removed by efficient antioxidant system in the body. Antioxidants are naturally occurring substances that when present at low concentrations compared to those of an oxidizable substrate significantly prevent or delays any oxidation of that substrate. They neutralize free radicals by donating one of their own electrons, ending the electron – gain interaction. The antioxidants nutrients themselves don't become free radicals by donating an electron because they are stable in either form. They act as scavengers, helping to prevent cell and tissue damage that could lead cellular damage and illness.[2] A wide range of antioxidants are effective in the body including enzymatic and non-enzymatic. The body produces different enzymes, including superoxide dismutase (SOD), catalase and glutathione peroxidase and glutathione reductase (GR). While the non-enzymatic defence consists of substances of low molecular weight such as reduced glutathione, vitamin C, Vitamin E, B-carotene, lutein, lycopene, Vitamin B12, Coenzyme Q10 and cysteine (an amino acid). Herbs such as bilberry, turmeric, grape seed or pine bark extracts and ginkgo can also provide powerful antioxidant protection for the body. Melatonin is a hormone secreted by pineal gland and proves to be powerful antioxidant and free radical scavenger [3].

CONCEPT OF AMA

The concept of ama is unique in Ayurveda, it finds place in genesis of almost all diseases and their management. The main cause of ama is agnimandya(impairment of agni). The first dhatu (rasa-nutrient portion of blood) which by the weakness of the fire (digestive activity) remaining uncooked (not digested, not properly processed) and becoming vitiated (bad, abnormal), accumulates in the amasaya(stomach) is known as ama. Others opines, that ama gets formed from intimate mixing with one another of greatly increased doshas just as poisons (get formed) from mixing of different kinds of kodrava [4].

Madava nidana defines ama associating itself with vata, moves quickly to the different seats of kapha in the body filling them and the dhamanis with waxy material. Thus, the bad end product of digestion associated with vata pitta and kapha in assuming different colours, blocks the tissue pores and passages with thick waxy material. It produces weakness and heaviness of heart, which becomes the seat of diseases[5]. Bhava prakasa defines ama as the matter which has not undergone vipaka, leading to durgandha(bad smelling), which is large in quantity, which is picchila(sticky) and leads to gatrasadana(weakness)[6]. Thus, in the absence of or due to the inhibition of kayagni, the food ingested is not properly digested and the products which arise out of such an impaired digestion being retained in the amasaya undergo such changes and yield toxic substances. This is called as ama.

So, the improperly digested rasa is ama (as per different classics) can be understood as Unprocessed food partially digested food or the matter which requires further parinama (transformation). Although ama is a wide entity, many similarities can be seen in the aetiology and properties of free radicals and ama.

Aetiology of ama

Ama is produced whenever there is malfunction of agni in the body. Similarly, free radicals are said to be produced in the body in abundance when equilibrium between its generation and body's primary defences are disturbed. The primary defences of the body include the activity of certain enzymes like superoxide dismutase, catalase and glutathione peroxidase. The impairment of these enzymes can lead to production of free radicals. The action of various enzymes can be considered as the action of agni. Therefore, it may be concluded that impairement of agni at cellular level causes the generation of free radicals.

Charaka describe the etiological factors as

1. Aharaja – abhojana, atibhojana, ajirnabhojana, visamasana , asatmyabojana, virudhabhojana etc, food qualities like *guru(heavy), sheeta(cold), ruksha(rough), suska(dry), vidahi, viruddha ahara* leads to the failure of digestion of even easily digestable food [7]. Similarly, food plays a role in free radical production. Free radicals are formed as natural byproducts of body's processes, including eating. Fats and oils become oxidised during storage because of exposure to light, air or heat. This creates free radicals and causes the unpleasant odours. On deep frying, they can become oxidised creating free radicals. Cooked and processed meats become oxidised when cooked at high temperatures. Preservatives used in processed meats also create free radicals. Processed foods frequently contain high levels of lipid peroxides, which produce free radicals that damage the cardiovascular system. Alcohols also increases the free radical production in the body.

2.Viharaja- sandharnata (suppression of natural urges), svapna viparyaya(keeping awakening in night and sleeping in days), atyambupana (drinking of water excessively) may give to amadosha – all these causes metabolic disturbances leading to oxidative stress and free radical production.

3.*Manasika* – consumption of food while afflicted mental upset due to kama krodha lobha moha irshaya, shoka(grief), bhaya(fear), lajja chintha(excessive thinking) are responsible for agnimandya[8].

All these *manasika* bhavas are responsible for creating stress in one's life. Mind is controlled by the vata i.e vata governs all mental activities such as perception, consciousness and the ability

of self-realization and psychological growth. Also, in the body vata governs the brain, nervous system, breathing circulation, digestion etc. Any disturbance in the manasika bhavas will cause disturbance in the sareerika bhavas. Stress increases the energy utilization which is mediated by hormones cortisol and catecholamines leading to increased production of free radicals. These hormones also themselves generate into destructive free radicals. Reactive oxygen species are formed as toxic waste in every cell at the time of energy production.

4.Miscellaneous- desha kala rtu vaisamya vyadikarshana (emaciation due to chronic diseases), also give rise to ama. Various sources of pollutions, various chemicals fertilizers, many radiations etc are a now a cause for desa kala and rtu vaisamyam. Various types of pollutants are now produced by the modern technologies which are harmful to the earth. These pollutants often generate free radicals in abundance. Moreover, the heavy use of farm chemicals and fertilizers in cultivation are also a source of free radicals. The food produced by using these chemicals generate free radicals while ingesting them. Cigarette smoking, alcohol drinking and all types of electromagnetic radiations are sources of free radical production. All these are causes for desha kala rtu vaisamya.

5.*Ama* with visha origin – ama is produced from visaja dravyas like biological toxin, gara visha, visha from viruddhahara etc [9]
Certain toxic substances like heavy metals produces free radicals. Auto oxidation, consequent inactivation of small molecules such as reduced thiols, flavins and electron transfer etc are few such processes by which free radical formation also goes on inside the body.
Free radicals are formed in each cell during energy production. The structural changes in the enzymes at the level of transcription or translation also leads to the production of free radicals. The functions of enzymes are like the functions of agni. Changes in agni or malfunctioning of agni leads to the production of ama. As their functions are alike, it is true that the impairment of agni at cellular level causes the generation of free radicals i.e ama.

Samprapthi

Susruta defines shad kriyakala, in the pathogenesis of diseases which are sanchaya, prakopa, prasara, sthanasamsraya, vyakthi and bheda. Ama sanchaya due to impairment of agni is the first step in disease causation.similarly, free radicals are produced due to the impairement in free radical scavengers. When sanchaya remains for long time, it leads to prakopa. Mild symptoms are produced during this stage. Next is the stage of prasara, where these accumulated ama moves from the position and goes to circulation. When it finds a suitable place which is weak, this ama lodges there and manifest as disease. This is called sthanasamsraya. Similar is in the free radical condition. Free radicals look for a site which is weak and can easily take part in electron exchange with them. The symptoms become more clear in this stage and if treatment is not given, it will lead to complications which is called bheda.[10].

Properties

Properties of ama include avipakam, asamyuktham, durgandham, bahupichilam *and* sadanam sarvagatranam. Avipakam indicates that ama exist in an incomplete metabolic state i.e. incompletely digested or metabolised form of food. Similarly, free radicals are an atom/molecule that contains one or more unpaired electron, which requires neutralization by antioxidants. Further, chakrapani says that once the dhatu vitiation occurs then the process of visamata continues to produce the visamadhatu which should be checked only by the chikitsa. The same phenomena are present in the free radical i.e. the continuity. The newly produced free radical is unstable in most cases and thus it will react with another molecule to produce another free radical. Next it is seen that when produced, free radicals are inassimilable to body components and exist in free state. Similar is the case with ama when it is produced it remains in inassimilable state and hence termed asamyuktam. Free radical cause damage to cell membrane and thus the cell is destroyed. This destruction may lead to purification and foul smell generations which are like one of the property of ama described as durgandham.

Though ama remains in the body as asamyuktham, but due to its properties like bahupicchilam etc, it sticks to normal healthy body tissues very quickly. Similar is the case with free radicals. To seek stability in their structure free radicals quickly attack the healthy molecules of the body and thus setting a chain reaction. The cells throughout the body are continuously exposed to these damaging molecules. Same has been described for ama as sadanam sarva gatrana[11].

ANTIOXIDANTS AND RASAYANA

Role of antioxidants include two prime aspects i.e. Preventive and chain breaking. Preventive will inhibit the initial production of free radicals. Chain breaking will inhibit the propagative phase of free radicals. Similarly, rasayana drugs also can be used in both curative and preventive aspect.

Charaka has described rasayanam to promote vigour and health. Chakrapani, the commentator of Charaka Samhita further extended the use of rasayanam to augment the recovery from disease process also. thus, rasayana can be used in both preventive aspect and in curative aspect. Susrutha has defined rasayanam as the method which retards the ageing process, prolongs longevity increases talent, vitality and makes the body fit to overcome the factors causing ailments. Rasayanam be considered as the solution for premature ageing. It is well known that in ageing DNA damage occurs. Rasayanam prevents oxidative stress induced damage to DNA. By rasayanam, the dhatu gets restored to the normal state, susceptibility to disease disappears, the body elements get aggrandized and the pace of age is slackened. Rasayana drugs offer longevity, improve memory, intellect, lustre and strength. Rasayana drugs also possess antioxidant activity and supress activity of oxidative stressors and thus reduce production of free radicals.

Ayurveda described various plants as rasayana such as amalaka, yastimadhu, aswagandha guduchi etc. these drugs enhances nutritional intake and qualities of dhatus which leads longevity, improves strength and ojobala. The rasayana drugs offer relief in stress, fatigue, early symptoms of ageing and autoimmune diseases. The antioxidant activity of these rasayana drugs are due to the presence of constituents such as vitamin C, carotene, riboflavin, tannins, gallic acid and polyphenols. It is believed that rasayana drugs increases the level of natural antioxidants, thereby reducing the risk of oxidative stress.

Antioxidant defense system against oxidative stress is composed of several lines, and the antioxidants are classified into four categories based on function.

A. First line of defense is the preventive antioxidants, which suppress formation of free radical

B.Second category: repair and de novo antioxidant (some proteolytic enzymes, repair enzymes of DNA etc)
These two can be correlated to the functions of rasayana

C.Third line of defense is the radical scavenging antioxidants suppressing chain initiation and/or breaking chain propagation reactions: radical scavenging antioxidants. This can be achieved by removing causative factors and can be taken as langana karma. If the chain reaction has already started, then use of certain substances which helps in neutralizing free radicals either by donating or accepting electrons from free radicals. This activity can be compared to pachana.

D.A fourth line is an adaptation where the signal for the production and reactions of free radicals induces formation and transport of the appropriate antioxidant to the right site. This is done using certain drugs which enhance the action of these enzymes. In other words, these are considered as dipana karma.

These langana pachana and dipana are the primary treatments of ama.

Many, Rasayana drugs have proven antioxidant properties in them. They also possess other properties like dipana pachana etc. Rasayana drugs with amaharana properties may be more useful in stress related conditions since many features of the free radicals can be correlated to the ama. Since these entities cannot be sharply correlated, all these possess similar properties in their function.

CONCLUSION

Stress is a major contributor of the modern lifestyle disorders in which oxidative stress and free radicals play a major role. Ama is not a single entity but is a generalised term which can be applicable for many malformed substances in the body and responsible for production of various diseases. Free radicals can be regarded under the category of ama. But ama comprises within itself a group of many such other harmful biochemical entities of which free radicals are just a part. Antioxidants are the substances that prevent the oxidation of molecules from free radicals, which function as both preventive and curative. Many rasayana drugs are deepana and pachana, which constitute the major treatment of ama. Moreover, they provide health and immunity delays, ageing process, prolongs longevity. All these functions can also be attributed to the antioxidants. Also, many rasayana drugs have proven antioxidant properties.

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