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A Conceptual Review on Free Radicals and Antioxidants through Ayurveda

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Pro-oxidants/oxidants, termed Reactive Oxygen species (ROS) and Reactive Nitrogen Species (RNS), are formed from both endogenous and exogenous sources. Free Radicals are central to both normal physiological functions and the development of various diseases, drawing substantial research focus. Free radicals have beneficial effects on body at lower levels and cause diseases at higher levels. Therefore, healthy state depends on the balance between free radicals and antioxidants in the body. This article explores the Ayurvedic perspective on the endogenous formation of free radicals through the roles of Jataragni, Bhutagni and Dhatwagni, and their relationship with Ama formation. Ama is a sequela of Agnimandya resulting from improper diet and lifestyle. As a defence mechanism, antioxidants help scavenge these free radicals. Article offers a conceptual review of the Ayurvedic insights into enzymatic endogenous antioxidants, non-enzymatic antioxidants such as metabolic antioxidants, nutrient antioxidants.

Keywords: Agnimandya, Ama, Antioxidants, Bhutagni, Dhatwagni, Free Radicals

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Introduction

Free Radicals are central to both normal physiological functions and the development of various diseases, drawing substantial research focus. These highly reactive, unstable molecules are potential threat to body leading to various diseases. A free radical can be defined as an atom or molecule containing one or more unpaired electrons in valency shell or outer orbit and is capable of independent existence. Free radicals are highly unstable and reactive due to the presence of unpaired electron which extract electron from other molecules, converting them into free radicals and perpetuating a chain reaction. Free radicals are the product of normal cellular metabolism. ROS (Reactive Oxygen Species) and RNS (Reactive nitrogen species) are two primary types of free radicals. They are derived from endogenous sources and exogenous sources and are referred to as pro-oxidants/oxidants.**[1]** Both ROS and RNS collectively constitute the free radicals and other non-radical reactive species. Non-Radical species are not free radicals but can easily lead to free radical reactions in living organisms.**[2]** **Free radicals and non-radical species** are as follows,

Free radicals	
Reactive Oxygen Species - ROS	
Radicals	**Non radicals**
Superoxide O2 •−	Hydrogen peroxide H2O2
Hydroxyl OH•	Singlet oxygen 1O2
Alkoxyl radical RO•	Ozone O3
Peroxyl Radical ROO•	Organic peroxide ROOH
	Hypochlorous acid HOCl
	Hypobromous acid HOBr
Reactive Nitrogen Species - RNS	
Radicals	**Non radicals**
Nitric oxide NO•	Peroxynitrite ONOO−
Nitrogen dioxide NO•	Nitrosyl cation NO+
	Nitroxyl anion NO−
	Dinitrogen trioxide N2O3
	Dinitrogen tetraoxide N2O4
	Nitrous acid HNO2
	Peroxynitrous acid ONOOH
	Nitryl chloride NO2Cl

Aim and Objectives

1. To establish a theoretical correlation between classical Ayurvedic concept and contemporary scientific understanding.

2. To establish correlation to enrich interdisciplinary insights and facilitate integrative interpretation.

Methodology

Concepts of *Ama, Agnimandya, Mala, Ahara Paka* are reviewed from classical Ayurvedic texts. Indexed journals and scientific literature are referred for information related to free radicals.

Ayurveda and Contemporary Review

Free Radical formation [3]

When cells use oxygen to generate energy, free radicals are created as a consequence of ATP production by mitochondria. These by-products are generally reactive oxygen species and as well as reactive nitrogen species that result from the cellular redox process.

Endogenous sources of free radicals include different organelles such as mitochondria, peroxisomes, endoplasmic reticulum. Exogenous sources of free radicals are alcohol, tobacco smoke, heavy metals, pesticides, high temperature, air and water pollution.

Agni, Ama

All the entities that are responsible for digestion and metabolism in body is termed as *Agni*. It is responsible for *Bala* (strength)*, Swasthya* (health)*, Upachaya* (nourishment).**[4]**

If *Agni* is hampered, the individual suffers from *Vikruti* (diseases).**[5]** *Bhutagni* is the one which transform or metabolise those components of *Ahara* (diet) that are homologous to them in their composition and structure. Metabolism in the tissue and cells is due to *Dhatwagni*.

Ahara Paka (digestion of food) forms two components **[6]**, *Prasada Bhuta* (nutrient component)- which is utilised in the body and *Mala Bhuta* (waste)- which is not utilised in the body.

Impairment in the *Agni* leads to formation of *Ama* (partially digested component/ by-product of metabolism) that is capable of causing diseases.

Ama **-** *Madhukosha* commentory of *Madhava Nidana* explains *Ama* as*, Mala Sanchaya* (accumulation of waste). It is quoted as *'Tatha Cha Apare- Ama Annarasam Kechit, Kechit Mala Sanchayam'.***[7]**

Discussion

Once overlooked, free radicals have now emerged as key biological entities, vital to normal cellular function yet implicated in the onset and progression of numerous pathological conditions. Free radicals are usually by-products of normal cellular metabolism. At low levels, have beneficial effects and on excessive accumulation have deleterious effects on molecular target sites like nucleic acids, proteins, lipids.**[8]**

The *Ahara* and *Vihara* in the today's era, that are potential endogenous sources for free radical formation, can be viewed from the *Nidanas* mentioned for *Ama*. *Bhutagni* and *Dhatwagni* are dependent on *Jataragni* (digestive fire). *Jataragni* is maintained from proper *Indhana* (fuel, that is *Ahara*).**[9]** Improper *Ahara* and *Ahara Vidhi* (dietary regimen) leads to *Agnimandya* and *Ama*. Free radicals also share same etiology.

Etiological Factors and its interpretation [10]

Ajeerna Ashana (eating before previous meal is digested)*, Ati-Bhojana* (over eating) can be understood as high calorie intake, which increases free radical. *Asatmya Ahara* (inconducive) as Westernized diet; *Guru Ahara* (heavy food) as refined foods, fried foods; *Sheeta* (cold)*, Ruksha Ahara* (dry) as frozen foods; *Sandushta Bhojanat* (contaminated food) as, processed foods, artificial colouring, flavouring, pesticides etc., which all have potential to increase free radical production the body. *Diwaswapna* (day sleeping)*, Ratrijagarana* (keeping awake at night) are causative factors for *Ama,* similarly, Sleep pattern influences free radical production.**[11]**

Desha Kala Ritu Vaishamya (abnormality in geographical region, time, season) as a causative factor can be understood as exogenous sources of free radicals like high temperature, air and water pollution.

Therefore, *Ama* which is a sequela of *Agnimandya* due to above mentioned *Nidanas* is a by-product of metabolism. So is the free radical which is the by-product of metabolism produced from endogenous and exogenous sources. As *Madhukosha* explains *Ama* as *Mala*, the *Mala* in the context of *Ahara Paka* leading to *Prasada Bhuta* and *Mala Bhuta*, is defined as *'Shareera Badhakaraha Malaha'* (that which causes destruction of body).

Also, is said to be *Shareera Upaghata Karaka* (harmful to body) while existing in the body. *Shareera Badhakara/ Shareera Upaghatakaraka* can be attributed to free radicals and can be understood as the deleterious effects of free radicals such as alteration in cell membrane, structures such as proteins, lipids, lipo-proteins, DNA, these also include formation of compounds that are cytotoxic and mutagenic.

Production of free radicals from endogenous sources can be understood through the simile mentioned- *"Kodravebhyo Vishayasyeva Vadayanti Amasya Sambhavan"* (*Ama* is formed in the body, as *Visha* (poison) develops in *Kodrava*-a type of millet).**[12]**

Antioxidants [13]

Antioxidants are classified as endogenous and exogenous antioxidants and also, as enzymatic and non-enzymatic antioxidants. Endogenous antioxidants include enzymatic antioxidants and non-enzymatic metabolic antioxidants. Exogenous antioxidants include non-enzymatic nutrient antioxidants. Enzymatic antioxidants are superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx). These have specific actions on specific radicals. Enzymatic antioxidants correlate with the *Bhutagni,* which also has specific actions on specific components. Free radicals formed from cellular metabolism (*Dhatwagni*) are acted upon by enzymatic antioxidants (*Bhutagni*).

Poshaka Rasa/ Prasada Bhuta Rasa (nourishing fluid) in this context, can be understood as endogenous metabolic antioxidants resulting from metabolism, possessing free radical scavenging activity. Nutrient antioxidants belonging to exogenous antioxidants can be viewed through the lens of *Rasayana Dravyas* (rejuvenating drugs) which are said to have anti-oxidant properties.

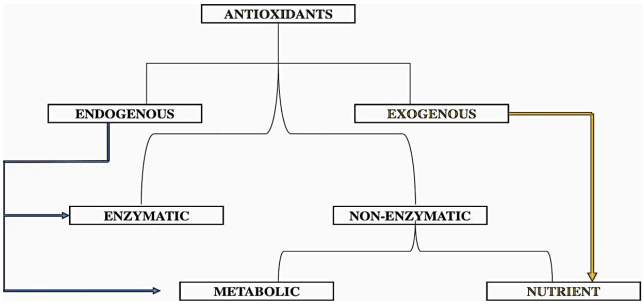
Lack of exercise, an unhealthy lifestyle can increase oxidative stress and the burden of chronic diseases. Hence *Viharaja Nidanas* (regimen) also play a role. Therefore, adopting *Vyayama* (exercise), proper dietary habits is essential.

Expulsion of *Mala* and enhancement of *Agni* can be achieved through *Shodhana Karma* (purificatory procedures). These actions correlate with elimination of free radicals (*Mala*)**[14]** and reduced production of free radicals by achieving proper metabolism (*Jwalanasya Deeptim*) respectively.**[15]**

Therefore, proper *Ahara* and *Vihara*, along with adherence to *Dinacharya, Ritucharya, Rasayana, Shodhana Karma,* plays a significant role in mitigating the harmful effects of free radicals.

Overview of the concept is outlined as,

Ayurveda correlation of free radical and their formation		
Dhatwagni and Bhutagni Mandya (due to Nidanas- Abhojana, Ati-Bhojana, Astamya Bhojana, Guru, Sheeta, Ruksha, Sandushta Bhojana, Ratri Jagarana, Divaswapna)	→	Dysfunction of Organelles like Mitochondria, peroxisomes, Endoplasmic reticulum.
Desha-Kala-Ritu Vaishamya	→	Exogenous sources for free radical formation- High temperature, air and water pollution.
Ama due to Agnimandya, is a by-product of metabolism.	→	Free radical is a by-product of cellular metabolism.
Ama is mentioned as Mala. Mala causes Shareera Baadha	→	Shareera Badha as Cellular stress/ oxidative stress having deleterious effect on protein, lipids, cell membrane, DNA. Radicals are cytotoxic and mutagenic.



Ayurveda correlation of antioxidants		
Bhutagni It has component/element specific action that are produced from Dhatwagni Paka.	→	Endogenous enzymatic antioxidant. They have target specific action on radicals produced from cellular metabolism.
Prasada Bhuta Rasa Produced as a result proper metabolism.	→	Endogenous metabolic antioxidants. Produced from the metabolism
Raasayana Dravyas	→	Nutrient antioxidants.

Conclusion

Agni is responsible for proper metabolism in body. Impairment due to *Aharaja* & *Viharaja Nidanas* leads to *Agnimandya* & formation of *Ama*. *Ama* is corelated with *Mala*, that which is *Shareera Baadhakara*. This correlates with impaired metabolism due to endogenous & exogenous etiological factors forming free radicals which have deleterious effects like oxidative or cellular stress on targets like nucleic acid, proteins & lipids.

Endogenous enzymatic antioxidants exhibit free radical scavenging activity which can be understood as a reflection of proper functioning of *Bhutagni*. Type of *Ahara* consumed plays a key role in either contributing to free radical formation or serving as a source of endogenous non-enzymatic metabolic antioxidants. *Rasayana* is viewed as a category of nutrient antioxidants. *Shodhana Karma* plays significant role in eliminating free radicals, enhancing and maintaining proper cellular metabolism. Therefore, proper *Ahara* and *Vihara*, along with adherence to *Dinacharya, Ritucharya, Rasayana, Shodhana Karma,* plays a significant role in mitigating the harmful effects of free radicals.

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