



Review Article

A REVIEW ON NOOTROPICS AND NUTRACEUTICALS: THE MISSILE FOR AGEING

Swati Shamrao Talokar *, Rohan Rajnikant Vakhariya, Vijay Rajaram Salunkhe, Chandrakant Magdum
Rajarambapu College of Pharmacy, Kasegaon.Tal- Walwa Dist.-Sangli Maharashtra, India

*Corresponding Author Email: swatitalokar@gmail.com

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ABSTRACT

Ageing is the process where structural and functional changes occur, in the living organisms during its life time. Age and age-related disease have a phenomenal impact on human life expectancy. Strategies have been developed to aware the people regarding how to stay fit and healthy as long as possible. Physical activity, healthy eating as well as staying integrated in the work life are elements of an active life. Along with physical activeness geriatrics need additional supplements which would compensate loss of energy that occurs due to ageing. Nutraceuticals, Nootropics are some of the approaches which would help them deal with ageing in proper manner. Present paper provides information of elements to age actively. It has discussion of the events that takes place during ageing, their consequences and role of Nutraceuticals, Nootropics in dealing with age and age related diseases.

Keywords: Active ageing, quality of life, Nutraceuticals, Nootropics

INTRODUCTION

Aging can be expressed as process of changes in the cells and tissues resulting in increased risks of disease and death. Ageing also means to grow and get mature along with progressive changes. Old age should be regarded as normal, unavoidable biological phenomenon¹. According to the United Nations Population Division the share of India's population of and above 60 yrs of age is projected to increases from 8 percent in 2010 to 19 percent in 2050. By mid-century, India's population over 60 yr of age is expected to be 323 million ².

There are many theories which explain aging processes. Theories include disease related factor, environment of the person, immune dysfunction, inborn defects, and free radical's mechanisms. A number of characteristic symptoms of ageing are experienced by a human. The symptoms such as cognitive impairment and neurodegenerative diseases like Alzheimer's disease, cerebrovascular disease, Parkinson's disease leads to isolation and possible depression³

Nootropics is a wide term which includes all kinds of food with health or medical effect. Various research works on these agents have revealed its importance in disease prevention and control. It has an important role as an anti-aging substance. This is by the virtue of its antioxidant activity which makes it a potent free radical scavenger in human physiological system. The free radicals are responsible for the generation of dead cells and gradually results in aging related disease. These are also found as a functional food and neuroprotectant ⁴

Signs of aging

Graying of hair is more apparent sign of ageing. Other key features are wrinkles and folds around the eyes, on the brow, around the mouth and in the regions of neck. The connective tissues, epithelial tissue and nerve tissues start showing changes.

Internal vital organs also age and the changes vary from organ to organ.

Aging and the heart

Maximal oxygen using capacity of the heart declines as it ages and as a result the maximal heart rate declines.

Aging and the brain

By the age of 40, brain loses approximately 10000 neurons and become nonfunctional. There is shrinkage in the brain matter called atrophy. Results are the diseases like Alzheimer's dementia etc

Effect of age on the eyes

By age of 50 years' problem of unclear vision appears in older people. There is a change in the capability to read small prints. The proteins in the lens mature and cataract and diminished vision occur. The elasticity of the lens in the eyes is decreased, which alters the capacity to focus clearly.

Aging in the liver and kidney

The capacity of liver and kidney to filter the waste material diminishes as we age. It is important to keep them free from Aging.

Age and the bones and joints

Due to wear and tear in the cartilages of knees and hips there is stiffness of the limbs occurs. This may also be observed in the back of the neck.

CAUSES BEHIND AGEING

Healthy ageing involves following three broad factors:

- 1. Social structural influences-**Gender, socioeconomic status, race, age.
- 2. Individual influences-** Psychological & behavioral.

3. Biological influences- Inflammatory & oxidative damage, damage to irreplaceable molecules, cells & blood metabolic hormone.

THEORIES OF AGEING

Free radical and Cross linking theory of ageing

Free radicals are chemical species that contains unpaired electrons. The most commonly found free radical in biological system is oxygen.⁶ Damage occurs when the free radical encounters a molecule to find an electron to pair its unpaired electron. The free radical often pulls an electron off a neighboring molecule, causing the affected molecule to become a free radical itself. Thus, a chemical chain reaction of radical production occurs.⁷ Such an event causes damage to the molecule and the cell becomes dysfunctional.

The chain reaction caused by free radicals leads to cross-linking of atomic structures. In cases, where the free radical-induced chain reaction involves base pair molecules in DNA, the DNA becomes cross-linked. Cross-linked DNA leads to various effects of aging, especially cancer. Cross-linking that occurs between fat and protein molecules leads to wrinkles. Free radicals can oxidize LDL and this leads to formation of plaque in arteries, leading to heart disease and stroke.

Error Theory: This theory is put forth by Sonneborn in 1979. He described that error can occur in the DNA transcription or in any step of protein synthesis; this may lead to actual death of a cell. The error would cause the reproduction of an enzyme or protein that was not a copy of the original. The next transcription would again contain an error. As the effect continued through several generations of proteins, the end product would not resemble the original cell and its functional ability would be diminished

Wear and tear theory: This theory was first proposed in 1882 by Weisman. Death of cells was seen as a result of tissues being worn out because they could not rejuvenate themselves. The theory also reflects a belief that organs and tissues have a preprogrammed amount of energy available to them and eventually wear out when the allotted energy is expended. Eventually, this leads to the death of the entire organism.⁸

Immunologic theory of ageing: According to the immunological theory, the immune system is programmed to decline over time and this is the main cause of aging. Immune system detects and destroys a wide variety of foreign agents, and preserves organism's healthy cells from destruction. In Immunosenescence there is decreased resistance to infectious diseases and hence chances of cancer are increased. As the result, the risk of death becomes significantly higher in elderly age.⁹

NOOTROPICS

Nootropics are also called as **cognitive enhancers**. These are drugs, supplements, or substances that improve cognitive functions like memory, creativity, or motivation. These are also used for enhancing concentration and memory capabilities. Cognitive enhancement involves following mechanisms such as:

1. Increasing circulation to the brain.
2. Providing chemical messengers to neurotransmitters
3. Providing usable energy to the brain.
4. Improving neuron function.
5. Preventing free radical and oxidative damage to brain cells and other cells.

Cognitive enhancers generally include

1. Adaptogenic agents
2. Natural antioxidants
3. Functional foods
4. Nutraceuticals
5. Dietary supplements

REMEDIES TO DEAL WITH AGEING

Following group of classes are used as anti ageing remedy:

Nutraceuticals

The term "Nutraceuticals" was formed by combination of "nutrition" and "pharmaceutical" by Dr. Stephen De Felice. Nutraceuticals are defined as "a food or part of food that provides medical or health benefits, including the prevention and/or treatment of a disease. The food products used as Nutraceutical are categorized as Probiotic, Prebiotic, Dietary fiber, Omega 3 fatty acid and Antioxidant.

Probiotics

Probiotics are fermented ingredients that allow specific changes in the composition and activity in the gastrointestinal micro flora. Probiotics confers benefits upon the host health. Numerous probiotic microorganisms e.g., *Lactobacillus rhamnosus* GG, *Lactobacillus reuteri*, bifidobacteria and certain strains of *Lactobacillus acidophilus* group are used in probiotic food. Probiotic supplementation increases quantity of natural killer cell and phagocytic activity. Probiotics by improving the nutritional and immune status helps in making up with the harmful effects of malnutrition in elderly people¹⁰

Prebiotics

Prebiotic are non-digestible food ingredients that when consumed in sufficient amounts, selectively stimulate the growth and activity of microbes in the colon, resulting in health benefits.

Antioxidants

The most common effect of antioxidants on the brain is their protective action against oxidative damage.

Action of antioxidants:

Antioxidants neutralize free radicals in the body. It has extra electron to share with unpaired free radicals. They get attached to free radicals so that they won't grab electron from other vital places. Antioxidants convert unstable & reactive free radicals to stable & underactive. In this way antioxidant stop damages of free radicals. They work as preventive and repair mechanism of cell¹¹

Anthocyanins, flavonoids, tannins, phenolic acids and stilbenoids¹²

Anthocyanins are present tremendously in Blackberry juice. Cyanidine-3-O-glucoside is active chemical constituent of blackberry. It has a protective effect against free radical-mediated endothelial dysfunction and vascular failure. Blackberries exert their protective effects directly by altering cell signals, calcium-buffering ability and neuroprotective stress. Berries are high in Flavonoids, condensed and hydrolysable tannins; Phenolic acids, Stilbenoids. These constituents confer antiproliferative, antioxidant and anti-inflammatory activities.

Polyphenols

They are also known as phenols. These are present in fruits and vegetables and help in brain functioning. They help to get rid of free radicals. The darker colored fruits and vegetables tend to be high in Phenolic, therefore possessing large antioxidant and anti-

inflammatory activity. Polyphenols retards and reverse elements of brain aging.

Dietary supplements

Dietary supplements increase glucose levels in the brain and hence influence memory, learning, concentration and decision-making. Lack of these leads to a negative effect on the brain. Examples of dietary supplements are Vitamins, Omega-3, Antioxidants, Amino acids, Caffeine, Iron.

Stimulants: One cup of green tea supplies high quantity of flavons. It has the highest antioxidant activity. Person who consumes green tea has lower risk of infections. Also chances of chronic degenerative conditions like cardiovascular disease, cancer, stroke, periodontal disease, and osteoporosis are reduced. Caffeine is shown to increase alertness.

Vitamins: Vitamins which have a significant contribution in brain function are Vit. B1, Vit. B12, Folic acid.

Vitamin-B1 and B12: Thiamine helps the body to convert carbohydrates into glucose. Glucose is what the brain uses as an energy source. Foods containing vitamin B1 include whole grains, rice, wheat germ; bran and organ meats. Cyanocobalamin and methylcobalamin both of them are used to make neurotransmitters. They maintain the nervous system by helping to metabolize fatty acids which are essential for the maintenance of myelin that surrounds nerves. Without sufficient Vitamin-B12 the ability to focus and think is reduced or even diminished. There are no dietary plant sources for it except Spirulina which is a bacterium. Soy and soy based products are a depletory of this essential vitamin.

Vitamin C and E: Vitamin C is a hydrosoluble vitamin; it acts as a strong antioxidant. Vitamin C is essential to prevent disease associated with connective tissue and to improve cardiovascular and immune cell functions. The main sources of vitamin C are broccoli, red paprika, pomegranate, acerola, citrus fruit, strawberry, tomatoes, and green vegetables in general. Vitamin E is an antioxidant which protects cellular membranes. Retinol helps cell to divide freely in the process of differentiation. Vitamin A is important for good vision and for prevention of eye diseases like glaucoma and cataract, which predominantly occur in old age. Vitamin A prevents penetration of microorganisms that cause disease by stimulating immunity. It is needed for bone, protein and growth hormone formation.

Amino acids: Many nutraceuticals contain these amino acids. They work by improving the nutritional and immune status. L-arginine also exerts antihypertensive and antiproliferative effects on vascular smooth muscles. Glutamine is considered a conditionally essential amino acid in metabolic stress.

Coenzyme Q10: Coenzyme Q10 hampers initiation and propagation of lipid peroxides. It also helps in regeneration of other antioxidants. Coenzyme protects from UV radiation damages and when applied locally on the skin or taken orally (dosage 60mg/day) decreases wrinkles. Its mechanism on the skin relies on the encouragement of collagen synthesis and skin restoration.

ADAPTOGENS

Adaptogens are defined as "class of natural origin which increases the ability of organism to adapt to environment and avoid damage from risk factors". Adaptogens decrease cellular sensitivity to stress. Adaptogens increase the resistance to stress which results in stress protection and prolong the phase of stimulation.

Certain plants which are believed to qualify criteria of adaptogens are:

1. Brahmi (*Bacopa monniera*)
2. Ginkgo (*Ginkgo biloba*)
3. Curcumin (*Curcuma longa*)
4. Amla (*Emblia Officinalis*)
5. Licorice (*Glycyrrhiza glabra*)
6. Ginseng roots (*Panax ginseng*)
7. Guggul (*Commiphora wightii*)
8. Ashwagandha roots (*Withania somnifera*)
9. Guduchi root/stem (*Tinospora cordifolia*),
10. Holy Basil (*Ocimum sanctum*)
11. Rhaponticum root (*Rhaponticum carthamoides*),
12. Shilajit (*Asphaltum bitumen*)

BRAHMI (*Bacopa monnieri*): *Bacopa monnieri* also known as Brahmi. *Bacopa monniera*, is a perennial herb¹³ having a small oblong leaves and purple flowers. The most important nootropic phytochemicals found in *Bacopa monnieri* is bacosides. It keeps the brain safe from free radical damage and stimulates learning and cognitive functioning. Other two most important alkaloids present in Brahmi are Brahmine and Herpestine. Bacoside A administration increases the activities of superoxide dismutase, catalase. Regular use of the Brahmi oil results in the prevention and cure of geriatric mental problems such as Amnesia and Alzheimer's disease. *Bacopa* possess anti-oxidant, hepatoprotective and neuroprotective activity.

GINKGO (*Ginkgo Biloba*): The leaves of this plant increase blood flow to the brain and also increase amounts of oxygen to the tissues. This herb improves brain glucose. An extract of ginkgo contains 24% flavones glycosides. It has been found to enhance mental functioning both in the young and old. Ginkgo components are active scavengers of free radicals which would result in premature death of cells. Its chemical constituents are mainly composed of three flavonols viz quercetin, keampferol and isorhamnetin, whereas terpenic derivatives are the ginkgolides A, B, C, J and M, and a sesquiterpenic trilactone called Bilobalide. Ginkgolides are antagonists of platelet-activating factor which reduces platelet aggregation and thus improves blood circulation. Bilobalide can reduce damage caused by brain ischemia and neuronal death.

CURCUMIN (*Curcuma Longa*): Curcuminoids present in Curcumin have the ability to improve mental function and act as neuroprotectors¹⁴. Curcumin protects the skin from harmful UV-induced effects by displaying antimutagen, antioxidant, free radical scavenging, anti-inflammatory, and anticarcinogenic properties. It is considered as a blood purifier for diseases such as dyspepsia, flatulence, liver disorders, arthritis, urinary tract diseases, wounds, jaundice, eye infections. It plays an important role in skin diseases such as acne and pemphigus.

AMLA (*Emblia Officinalis*): *Emblia Officinalis* also called as Amla is a deciduous tree from Phyllanthaceae family. Amla churn possesses memory enhancing action and it is a proven remedy in management of Alzheimer's disease. This memory enhancing activity of Amla is due to its property of reducing brain cholinesterase and total cholesterol levels.

LIQUORICE (*Glycyrrhiza Glabra*): Liquorice is the root of *Glycyrrhiza glabra*. It belongs to family Fabaceae. The roots and rhizomes of *Glycyrrhiza glabra* is an efficient brain tonic. It also balances the sugar levels in the blood. The main constituent of *Glycyrrhiza glabra* is glycyrrhizin. The protective effect of liquorice may be due to its antioxidant property. Anti-oxidant property causes reduced brain damage and improved neuronal function and hence enhances memory.

GINSENG (*Panax Ginseng*): This herb has an anti-stress effect. It exerts antioxidant and steroid metabolism activity on the hypothalamus-pituitary-adrenal endocrine function. It stimulates activities in the brain to increase release of body energy. This causes increased work output. Ginseng root are characterized by the presence of ginsenosides. Ginsenosides have ability to increase the body's resistance to stress, trauma, anxiety and fatigue by modulating the immune function. It improves memory, learning performance, motor activity and as aphrodisiac, ginseng can be applied to patients with sexual dysfunction.

GUGGUL (*Commiphora Wightii*): Commiphora wightii is a flowering plant of the family Burseraceae. The active ingredient

in the extract is the steroid guggulsterone, which acts as an antagonist of the farnesoid X receptor. Gugulipid has significant protective affect against memory deficits model of dementia. This can be attributed to anti-oxidant and anti-AChE activity of Gugulipid which makes Gugulipid a potential anti-dementia drug.

Ethanol extracts of *Glycyrrhiza glabra*, *Curcuma longa* (roots), seeds of *Psoralea corylifolia*, *Cassia tora*, *Areca catechu*, *Punica granatum*, fruits of *Embellica officinale*, leaves of *Centella asiatica*, dried bark of *Cinnamon zeylanicum*, and fresh gel of *Aloe vera* in varied concentrations showed improvement of the viscoelastic and hydration properties of the skin. These beneficial effects might be due to the synergistic antioxidant.

Table 1: Features and consequences of normal ageing⁵

System	Changes with ageing	Clinical consequence
Central nervous system	Loss of neuronal, degeneration of cochlear, loss of opacifcity	Increase risk of confusion, High peach of hearing, cataract
Respiratory system	Reduced lung elasticity	Reduced expiration flow, Reduction in vital capacity
Cardiovascular system	Reduced heart rate and decreased elasticity of aorta	Increased risk of postural hypotension.
Endocrine system	Reduced sensitivity to insulin	Risk of impaired glucose tolerance
Renal system	Reduced glomerular filtration rate and tubular function	Impaired fluid balance, drug metabolism and excretion.
Gastrointestinal system	Reduced motility	Constipation
Bones	Low bone density	Osteoporosis

CONCLUSION

Nutraceuticals have been playing a important role in the prevention of human diseases. They have all round role of antioxidant, neuroprotectant as well as functional food. Antioxidants derived from natural source are generally used for the manufacturing nutraceuticals. These sources or supplements prove to be a better functional food. The nutraceuticals have very little or negligible side effects in comparison to its profound effect on the cell metabolism. These features of nutraceuticals make it a potent food substance to be used by not only by geriatrics but also by younger generation.

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