The effect of comfort capsule, an ayurvedic medicine, on free radicals and antioxidants in disease and health

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Abstract
The free radicals and oxidants can be both damaging and beneficial to the organism; they play a dual role as toxic and beneficial molecules. They come from either in-situ cell metabolism or external sources (pollution, cigarette smoke, radiation, medication). The accumulation of free radicals in the body causes oxidative stress when they cannot be eliminated gradually. Cancer, autoimmune disorders, aging, cataract, rheumatoid arthritis, cardiovascular, and neurological illnesses are all influenced by this mechanism. Antioxidants, which are either naturally created in the body or externally supplied by foods and/or supplements, are one of numerous processes by which the human body combats oxidative stress. This brief overview examines the taxonomy, mechanisms of formation and catabolism of free radicals, their beneficial and deleterious effects on cellular activities, the potential role of antioxidants in preventing and repairing oxidative stress-related damage, and the role of antioxidant supplementation in health maintenance. The herbs in the comfort capsule have a dual function: they reduce oxidative stress while also encouraging normal cell proliferation and growth and avoiding cell death. Herbs are being studied for their involvement in oxidative stress and free radical generation, as well as normal cell growth and prevention.

Keywords: Autoimmune disorders, Cardiovascular, degenerative illness and Rheumatoid arthriti

Introduction

The element oxygen is required for life to exist. As a result of the mitochondria's generation of ATP (adenosine triphosphate), free radicals are generated when cells use oxygen to generate energy. The cellular redox process produces reactive oxygen and nitrogen species (ROS and RNS). These organisms have a dual function as harmful and helpful substances. The careful balance between these two opposing impacts is undeniably crucial in life. ROS and RNS have a positive impact on cellular responses and immunological function when present in low to moderate amounts. They cause oxidative stress at high doses, which is a harmful process that damages all cell structures.[1-10] Cancer, arthritis, aging, autoimmune disorders, cardiovascular and neurological diseases all have oxidative stress as a contributing factor. Antioxidants, which are either naturally created in the body or externally supplied by foods and/or supplements, are one of numerous processes by which the human body combats oxidative stress. Antioxidants, both endogenous and exogenous, act as "free radical scavengers," preventing and repairing damage produced by ROS and RNS. As a result, they can boost immunological defense and reduce the risk of cancer and degenerative diseases.[11-15]

Characteristics of free radicals and oxidants

Free radicals and other non-radical reactive derivatives, also known as oxidants, are referred to as ROS and RNS. Radicals are less stable than non-radical species, despite their higher reactivity. A free radical is a molecule that has one or more unpaired electrons in its outer shell.[1-5] Free radicals are created when a chemical link is broken in such a way that each fragment retains one electron, when a radical is cleaved to produce another radical, and when redox reactions occur.[1-2] Hydroxyl (OH), superoxide (O_2), nitric oxide (NO), nitrogen dioxide (NO_2), peroxyl (ROO), and lipid peroxyl are all examples of free radicals (LOO). Also, while hydrogen peroxide (H_2O_2), ozone (O_3), singlet oxygen (O_2), hypochlorous acid (HOCl), nitrous acid (HNO_2), peroxynitrite (ONOO), dinitrogen trioxide ($N2O_3$), and lipid peroxide (LOOH) are not free radicals, they can easily cause free radical reactions in living organisms.[8] Biological free radicals are thus highly unstable molecules with accessible electrons to react with a variety of chemical substrates such as lipids, proteins, and DNA.

Generation of free radicals and oxidants

Enzymatic and non-enzymatic processes can both result in the formation of ROS and RNS in cells. The respiratory chain, phagocytosis, prostaglandin synthesis, and the cytochrome P450 system are all examples of enzymatic reactions that generate free radicals.[1-9] Several cellular oxidase systems, such as NADPH oxidase, xanthine oxidase, and peroxidases, for example, create the superoxide anion radical (O_2). Once generated, it undergoes a series of reactions that produce a variety of ROS and RNS, including hydrogen peroxide, hydroxyl radical (OH), peroxynitrite (ONOO), hypochlorous acid (HOCl), and others. A number of oxidase enzymes, including amino acid oxidase and xanthine oxidase, create $H_2 O_2$ (a non-radical). The oxidation of hypoxanthine to xanthine and xanthine to uric acid is catalyzed by the last one. The interaction of O_2 with $H_2 O_2$ in the presence of Fe2+ or Cu+ produces the most reactive free radical in vivo, the hydroxyl radical (OH) (catalyst). The Fenton reaction is the name given to this reaction.[3-8] Myeloperoxidase, a neutrophil-derived enzyme that oxidizes chloride ions in the presence of H_2O_2, produces hypochlorous acid (HOCl). The oxidation of L-arginine to citrulline by nitric oxide synthase results in the formation of nitric oxide

radical (NO-) in biological tissues.3-8 Ionizing radiations, as well as non-enzymatic interactions of oxygen with organic molecules, can produce free radicals. The non-enzymatic process can also occur in the mitochondria during oxidative phosphorylation (i.e. aerobic respiration).[4,5,8] Endogenous and external sources both produce ROS and RNS. Inflammation, emotional stress, excessive exercise, ischemia, infection, cancer, and aging all produce endogenous free radicals. Air and water pollution, cigarette smoke, alcohol, heavy or transition metals (Cd, Hg, Pb, Fe, As), some medications (cyclosporine, tacrolimus, gentamycin, bleomycin), industrial solvents, cooking (smoked meat, used oil, fat), and radiation are all examples of exogenous ROS/RNS.[4-14] these exogenous chemicals are degraded or converted into free radicals when they penetrate the body through various mechanisms.

Beneficial activities of free radicals and oxidants

ROS and RNS are needed for the maturation of cellular structures at low to moderate concentrations and can be used as weapons by the host defense system. As part of the body's defense against sickness, phagocytes (neutrophils, macrophages, and monocytes) generate free radicals to eliminate invading pathogenic bacteria.[5,10] Granulomatous disease patients are a good example of the importance of ROS generation by the immune system. These patients have a membrane-bound NADPH oxidase system that is faulty, preventing them from producing the superoxide anion radical (O_2), resulting in multiple and persistent infections.[4-5] The physiological roles of ROS and RNS in the function of a number of cellular signaling systems are also favorable impacts of ROS and RNS.[7-9] Nonphagocytic NADPH oxidase isoforms produce them, and they play an important role in the regulation of intracellular signaling cascades in fibroblasts, endothelial cells, vascular smooth muscle cells, cardiac myocytes, and thyroid tissue. Nitric oxide (NO), for example, is an intercellular messenger that regulates blood flow, thrombosis, and brain function.[7] NO is also crucial for non-specific host defense as well as the destruction of intracellular infections and malignancies. The production of a mitogenic response is another advantageous property of free radicals.[7-8] In conclusion, low or moderate levels of ROS/RNS are essential for human health.

Deleterious activities of free radicals, oxidants and Pathogenes.

When free radicals and oxidants are created in excess, they cause oxidative stress, a harmful process that damages cell membranes and other components like proteins, lipids, lipoproteins, and deoxyribonucleic acid (DNA).[5-10] When cells are unable to efficiently remove the excess free radicals produced, oxidative stress can occur. In other terms, oxidative stress is caused by an imbalance in the creation and neutralization of reactive oxygen species (ROS/RNS). Excess hydroxyl radical and peroxynitrite, for example, can cause lipid peroxidation, which damages cell membranes and lipoproteins. Malondialdehyde (MDA) and conjugated diene molecules, both of which are cytotoxic and mutagenic, are formed as a result of this process. Lipid peroxidation is caused by a radical chain reaction, which spreads quickly and impacts a large number of lipid molecules once it begins.[14] ROS/RNS can potentially cause structural changes in proteins, as well as a loss of enzyme activity.[9,14] The creation of various oxidative DNA lesions as a result of oxidative DNA damage might result in mutations. The body uses DNA repair enzymes and/or antioxidants to combat these attacks.[6-9] Oxidative stress can cause a number of chronic and degenerative disorders, as well as the aging process and some acute pathologies, if it is not adequately managed (trauma, stroke).

Antioxidant Process

An antioxidant becomes oxidized when it kills a free radical. As a result, the body's antioxidant supply must be replenished on a regular basis. As a result, whereas an antioxidant may be effective against free radicals in one system, it may lose its effectiveness in other systems. An antioxidant can also act as a pro-oxidant in some situations, such as when it produces hazardous ROS/RNS.[10] The antioxidant process can work in one of two ways: it can break chains or it can prevent them from breaking. When a radical releases or steals an electron, a second radical is generated, which is known as chain-breaking. The last one repeats the process on a different molecule until either the free radical generated is stabilized by a chain-breaking antioxidant (vitamin C, E, carotenoids, etc.) or it disintegrates into an innocuous product. Lipid peroxidation is a classic example of a chain reaction like this. Antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase can inhibit oxidation by slowing the commencement of chains, for example, by scavenging initiating free radicals or stabilizing transition metal radicals like copper and iron.[10]

Neurological disease and oxidative stress

Alzheimer's disease, Parkinson's disease, multiple sclerosis, amyotrophic lateral sclerosis (ALS), memory loss, and depression are among the neurological illnesses for which oxidative stress has been studied.[17-20] Numerous experimental and clinical studies have shown that oxidative damage is a major factor in the loss of neurons and progression to dementia in diseases like Alzheimer's.[19] Oxidative stress causes the development of ß-amyloid, a toxic peptide commonly seen in Alzheimer's sufferers' brains.[20]

Nephropathy and oxidative stress

A range of renal disorders, including glomerulonephritis and tubulointerstitial nephritis, chronic renal failure, proteinuria, and uremia, are linked to oxidative stress.[5,27] Certain medicines, such as cyclosporine, tacrolimus (FK506), gentamycin, bleomycin, and vinblastine, cause nephrotoxicity due to oxidative stress caused by lipid peroxidation.[27-30] Heavy metals (Cd, Hg, Pb, As) and transition metals (Fe, Cu, Co, Cr) cause various forms of nephropathy and carcinogenicity in the body.[11-12]

Antioxidants and health maintenance

Antioxidants either naturally produced in situ (endogenous antioxidants) or externally provided through foods are one of the body's methods for combating oxidative stress (exogenous antioxidants). Antioxidants help to prevent disease by neutralizing excess free radicals, protecting cells from their damaging effects, and neutralizing free radicals.[20]

Role of Free radical role in cell injury

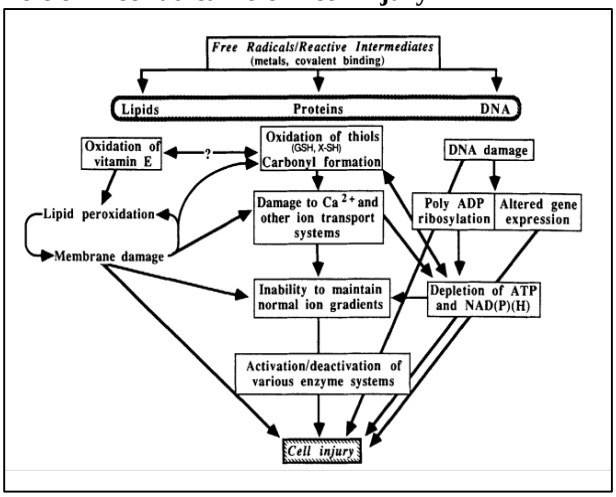

Figure 1. Free radicals cause cell damage through a variety of mechanisms. Because free radicals can interact with lipids, proteins, and DNA, they can cause a variety of alterations that can impact cell function. This figure depicts the alterations that are thought to be the most likely cause of harm.[21]

1. Mechanism of Tissue injury and inflammation

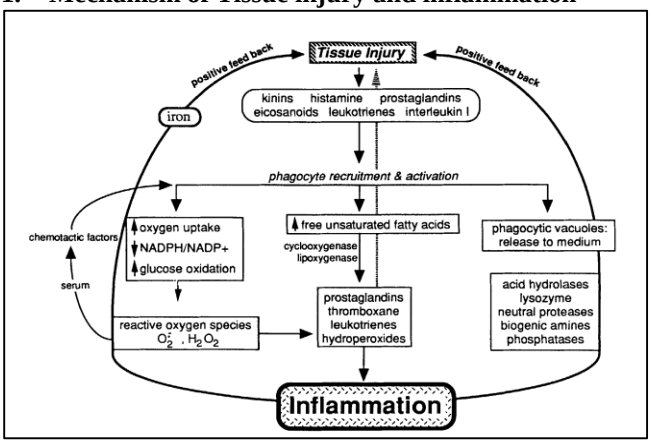

Figure 2. Inflammation and free radicals. The inflammatory process is a complicated series of events involving several chemical mediators. A component of the entire response, including the formation of chemotactic factors, appears to be influenced by reactive oxygen species. The generation of reactive oxygen species (ROS) contributes to the tissue damage associated with chronic inflammation.[21]

2. **Ashwagandha** ***(Withania somnifera)***, this valuable medicinal plant, also known as (winter cherry), has been used in Ayurvedic and indigenous medicine for 3000 years. Ashwagandha is also known as Indian ginseng by certain herbalists. Many bioactive chemicals found in the plant extract include antioxidant, neuroprotective, anti-stress, anti-inflammatory, and immunomodulatory properties. Arthritis, impotence, amnesia, anxiety, cancer, neurodegenerative and cardiovascular illnesses, and others are among the ailments for which the plant extracts and its bioactive compounds are employed in the prevention and therapy. It was able to lower reactive oxygen species levels, adjust mitochondrial activity, control apoptosis, and improve endothelial function. It has been used to treat a variety of chronic problems involving the nervous system. Molecularly, ashwagandha root was beneficial in Alzheimer's disease (AD) by reducing nuclear factor-kB activation, limiting amyloid beta (A) generation, restoring synaptic function, and increasing antioxidant effects through the migration of Nrf2.[22]
3. **Brahmi** ***(Bacopa monnieri)*** is a creeping perennial native to Australia and India with small oblong leaves and purple blooms that grows in warm wetlands. Antioxidant neuroprotection (through redox and enzyme induction), acetylcholinesterase inhibition and/or choline acetyltransferase activation, -amyloid reduction, improved cerebral blood flow, and neurotransmitter modulation are some of the methods by which BM works (acetylcholine [ACh], 5-hydroxytryptamine [5-HT], dopamine [DA]). At conventional concentrations, the milieu of nootropic phytochemicals present in Bacopa monnieri (BM), notably triperpenoid saponins known as bacosides, have minimal visible deleterious effects. Antioxidant, hepatoprotective, and neuroprotective properties of BM have been discovered. New study suggests that acetylcholinesterase inhibition, choline acetyltransferase activation, -amyloid reduction, improved cerebral blood flow, and monoamine potentiation are all possible mechanisms of action. Free radicals (chemical species with unpaired electrons produced during normal metabolism) overpower the cell's homeostatic defensive mechanisms, resulting in oxidative stress (OS). Superoxide dismutase, catalase, glutathione peroxidase (GPx), glutathione reductase (GSR), and other free radical–quenching enzymes are among them. Antioxidant substances such as vitamins A, C, and E, as well as a variety of phytonutrients, serve an important protective role (particularly phenols). By degrading ligands, peroxidizing lipids, altering metabolic pathways, denaturing proteins, and breaking DNA strands, OS has a role in many illnesses, including aging. Because it is metabolically active, has significant quantities of pro-oxidant iron, and is made up mostly of unsaturated lipids, the brain is particularly vulnerable to OS (prone to lipid peroxidation). Furthermore, many exogenous anti-oxidants are unable to quench reactive oxygen species (ROS) in the brain due to the blood–brain barrier.[23]
4. **Jatamansi** ***(Nardostachya jatamansi)*** Nardostachys jatamansi roots have been used in Ayurvedic medicine for anti-ischemic, antioxidant, anticonvulsant, and

neuroprotective properties. As a memory booster, the N. jatmansi. It also restored aging-induced forgetfulness in mice, which was caused by natural aging.

Because scopolamine-induced amnesia was reversed, it's probable that the memory improvement was due to cholinergic transmission in the brain being facilitated. As a result, N. jatmansi could be a valuable memory-restoring agent in the treatment of dementia in the elderly. Its antioxidant property is thought to be the underlying mechanism of action.[24]

5. **Amrita (*Tinospora cordifolia)*** Guduchi is another name for Guduchi. It's most widespread in India and China. Ayurveda and folk medicine employ the plant alone or in combination with other plants. Plant phytochemicals (alkaloids, terpenoids, lignans, steroids, and so on) bestow a wide range of pharmacological qualities to the plant, including antioxidant, antibacterial, antidiabetic, antistress, anticancer, antiHIV, and immunomodulatory properties. The Chloroform fraction of T. cordifolia (TcCF) contains pharmacologically active chemicals such rutin and quercetin, which provide anticancer qualities to the plant against breast cancer cells (MDA-MB-231 and MCF 7). It has anti-oxidant, anti-stress, neuroprotective, and immunomodulatory characteristics that aid learning, memory, and recall while also providing significant brain nourishment. Assist in the promotion of mental well-being and functionality. It can aid to increase memory and problem-solving abilities in times of everyday stress.[25]
6. **Sarpagandha (*Rauwolfia serpintina*)** Rauwolfia serpentina (Indian Snakeroot) is a possible source of phytopharmaceuticals for treating insomnia, and it is well-known for therapeutic applications and the production of traditional beverages. Many important pharmacological actions are attributed to its various alkaloids, including the main root alkaloid reserpine. R. serpentina phytochemical investigations found that the plant is a rich source of secondary metabolites such as phenols, favonoids, and alkaloids, as well as saponins, tannins, terpenes, steroids, reducing sugars, and fatty acids. R. serpentina, on the other hand, has been extensively researched for its alleged medicinal effects of indole alkaloid components, particularly the alkaloid reserpine. The wonder plant R. serpentina's multipotent medicinal benefits received early attention for pharmacological studies. As a result of the positive results in pharmaceutical-clinical investigations, this plant has become a prospective natural medication source. Anti-oxidative, anti-inflammatory, anti-bacterial, anti-fungal, anti-venomous, gastroprotective, hypolipidemic, hypoglycemic, hepatoprotective, antidiabetic, cardioprotective, anti-hypertensive, neuroprotective, nerveregenerative, sedative, anti-prostate cancerous, antidiabetic, cardioprotective, anti-hypertensive, cardioprotective, anti-hypertension Nonetheless, Wilkins (1954), who reported an overall good psychological change, firmly supported the nervine property of R. serpentina.[26]
7. **Shankhpuspi (*Convolvulus pluricaulis)*** Bioactive components such as cinnamic acid, pentanoic acid, ascorbic acid, vitamin E, phthalic acid, squalene, silane, decanoic acid, linoleic acid, -sitosterol, tropane alkaloids, kaempferol, and others have been widely employed in Ayurvedic and Unani medicine. The brain is an incredible, incredibly complicated organ in the human body that contains millions of mitochondria that are susceptible to free radical damage. Oxidative stress is caused by an imbalance between oxidants and antioxidants in the cells, which leads to cellular damage. Reactive oxygen species (ROS) are oxidative radicals such as hydroxyl radical (OH), superoxide anion (O_2), and hydrogen peroxide (H_2O_2) that are constantly created in cells as a result of normal metabolic activities. Where the oxidants within the cell exceed than the levels of antioxidants present, causes macromolecules such as DNA, protein and lipid damage. These macromolecules damage is observed in several diseases such as diabetes, ischemia/reperfusion and neurodegenerative diseases such as Parkinson's, Huntington's and Alzheimer's disease, hypertension. Antioxidant supplementation protects against reactive oxygen species-mediated cell damage. Several medicinal plants are used to treat various diseases that are also a rich source of natural antioxidants such as flavonoids, polyphenols, and terpenoids.[27]
8. **Marich (*Piper nigrum)*** It is one of the most widely used spices in the world, and it is also used in many cultures' folk medicinal practices. Piperine, a primary alkaloid found in black pepper (Piper nigrum L.), has long been used as a condiment and flavoring in savory meals. Piperine has anti-inflammatory, anti-convulsant, antioxidant, anti-depressant, and cognitive-enhancing properties. Piperine has been shown to protect against neurodegeneration and cognitive impairment in an animal model of Alzheimer's disease-like cognitive deficits (AD). The plant extracts dramatically improved memory performance while also having antioxidant properties. It is claimed that the plant extract reduces oxidative stress in the hippocampus, thus alleviating amyloid beta-induced spatial memory impairment.[28]

Conclusion

Antioxidant therapy appears to be a promising standard treatment because of the role of oxidative stress in the etiology of various chronic and degenerative diseases. In the future, a therapeutic strategy aimed at increasing cell antioxidant capacity could be employed to strengthen long-term therapy effectiveness. Many questions about the use of antioxidant supplements in disease prevention, however, remain unanswered. Before this treatment may be formally suggested as an adjuvant therapy, more research is required. Meanwhile, it is vital to remember that avoiding oxidant sources (cigarettes, alcohol, bad food, stress, etc.) is just as important as eating an antioxidant-rich diet. Indeed, our health is influenced by the way we live. Comfort capsule is a natural cure medicine which contains important herbs such as

Ashwagandha (*Withania somnifera*) 125 mg, Brahmi (*Bacopa monnieria*) 125 mg, Jatamansi *(Nardostachya jatamansi)* 50 mg, Amritha (*Tinospora cordifolia)* 50 mg, Sarpagandha (*Rauwolfia Serpintina*) 75 mg, Shankhpuspi (*Convolvulus pluricaulis)* 50 mg, Marich (*Piper nigrum)* 25 mg which exhibits anti-inflammatory, neuroprotective, anti-stress, antioxidant, immunomodulatory and rejuvenating properties, with no risk of side effects and works directly on the causes of ailments to eliminate them from your body and help in boost memory, reduce stress, anxiety, sadness, and sleeplessness.

Acknowledgement
Authors are thankful to Surya Krishna Shrestha**,** production director, Dekha Herbal Pvt. Ltd, Dhapakhel 23, Lalitpur, Kathmandu, Nepal for providing facilities for the successful completion of the study and I would like to express my love to loveable and respectable Babugee Mr. Samsulhak Miya and Aama Ms. Jaisul Nesha for motivation. Token of gratitude to Purnima Kapali.

Source of Funding
None

Conflict of Interest
None.

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How to cite: Kamrudeen S, Krishna S S et al. The effect of comfort capsule, an ayurvedic medicine, on free radicals and antioxidants in disease and health *IP Int J Aesthet Health Rejuvenation* 2021;4(4):.68-72