REVIEW

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Cancer versus anticancer factors: A review of these factors, health impacts, and awareness

Uttam Chowdhury[1*], Shreya Chowdhury[1]

[1]*The University of Arizona, Tucson, AZ, 85721, United States*

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ABSTRACT

Dr. Uttam Chowdhury, Ph.D.

Dr. Uttam Chowdhury, Ph.D.,is a renowned researcher in the field of arsenics. He worked in the Department of Molecular and Cellular Biology at the University of Arizona, USA (2003-2010) as an Assistant Research Professor/Researcher/Co-PI with a renowned Toxicologist named Prof. H. Vas Aposhian. With a Ph.D. in Science from SOES (School of Environmental Science), Jadavpur University, India, under the supervision of Dr. Dipankar Chakraborti, one of the world-famous scientists on the field of arsenic research, Dr. Chowdhury has made significant contributions to the field of environmental science on arsenic research. His scholarly output includes over 90 research articles in peer-reviewed journals, book chapters, conference papers and abstracts, with publications in prestigious journals such as Nature. Uttam Chowdhury's enormous scientific merit is demonstrated through 6810 citations (25 publications cited more than 50 times and one publication cited more than 1320 times), 39931 reads, 3354 research interest score, and an h-index of 34 till today, January 31, 2024 (Source: ResearchGate and Google Scholar). One of his publications has been reported as entitled “Arsenic in Asia-Water at Its Worst” on the “Science Selections” in the EHP journal (May 2000, Volume 108, Number 5, Page A 224) by Karen Breslin. This topic was also selected and used as the cover page of this journal (EHP, May 2000, Volume 108, Number 5).

Dr. Chowdhury's research has been recognized with several awards and fellowships, including a Research Fellowship in 2002 at the National Institute for Environmental Studies (NIES), MinistryoftheEnvironment, Japan, focusing on environmental planning for global environment protection. He also received Research Fellowships in 2001 and 2000 from the National Institute of Health Sciences (NIHS), MinistryoftheEnvironment, Japan, dedicated to maintaining global environmental protection.

A recipient of the Jawaharlal Nehru Scholarship (2000-2001) for Doctoral Studies and the Award of Research Fellowship (1999-2001) from the University Grand Commission in New Delhi, India. Dr. Chowdhury has also been acknowledged for his academic excellence with a place on the Dean’s Honor List at Dhaka University, Bangladesh, from 1985 to 1996. He has completed his B.S. (Honors) and M.S. from the Department of Biochemistry at the Dhaka University, Bangladesh.

In addition to his research achievements, Dr. Chowdhury is an experienced mentor and leader. He has extensive experience in training and managing undergraduate and graduate students, visitors from national and international institutes/universities', along with postdoctoral fellows in laboratory practices. As a lab manager and researcher, he has overseen the operation of the Geochemistry Lab under the Geochronology and Thermochronology program in the Department of Geosciences at the University of Arizona, USA since 2010, supervising over 25 student workers and employees. He had also guided more than 30 field assistants in sample and data collection under the "water and sanitation programs" with different research projects funded by ADB, UNICEF, USAID, IDA, DFID, SDC, etc., in different areas of Bangladesh between 1994 and 1998 when he was a Research Officer in the Environmental Health Program (EHP) at the International Center for Diarrheal Disease Research, Bangladesh (ICDDR, B), Dhaka, Bangladesh.

Dr. Chowdhury is a respected instructor, leading intensive summer workshops at the University of Arizona. His professional memberships include the Society of Toxicology (SOT), American Society for Mass Spectrometry, American Chemical Society (ACS), and the New York Academy of Sciences (NYAS), USA, underscoring his commitment to the broader scientific community.

The abstract of this article

Cancer is a disease that is caused when cells begin to divide without stopping and spreading into surrounding tissues by any changes or damage to DNA. Most cancer disease cases are due to environmental risk factors, and many of these factors are controllable lifestyle choices.

Free radicals are risk factors that cause cancer, but antioxidants are anti-risk factors that work as anticancer and protect our health from diseases like cancer. It would be very important to know how these risk and anti-risk factors work, and how we could maintain and protect our health.

Free radicals (FRs) have an unpaired electron in their outer orbit that make them very unstable because they want to keep pair of electrons in their outer orbit, and their reactivity is very strong for that missing electron to become stable. Due to that, FRs attack healthy/normal cells for electrons that they can find to become stable. Free radicals could take electrons from DNA molecules, proteins, fats, carbohydrates, and other molecules, damaging and turning them into new free radicals. In this process, free radical chain reactions damage the entire cell, then their neighbors, and so on. Having too many free radicals in the body increases the likelihood of damage to healthy cells. This

resulting damage is called oxidative damage.

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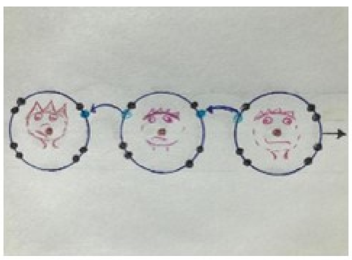
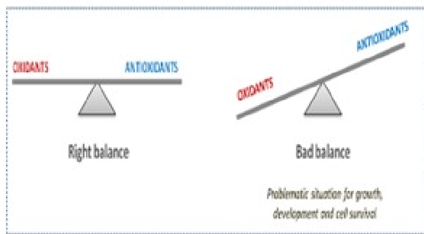
Tel.: +1-(520)-820-5861; e-mail: ukchowdh@arizona.edu

Free radicals may play a role in cancer, inflammations, diabetes, heart disease, brain diseases, lung diseases, kidney diseases, eye diseases, joint pain, stroke, Alzheimer's, Parkinson's, other age-related diseases, disorders, etc. However, an antioxidant is a molecule that inhibits the oxidation of other molecules like free radicals by donating electrons, in which they become stable, stop more free radicals' production, and prevent free radical damage. Under this process, the most benefited result is that FRs become stable, but antioxidants do not become free radicals and leading people to remain healthy.

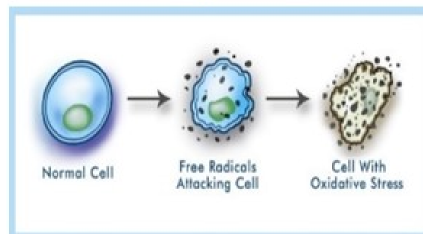
FR chain reactions



Oxidative stress

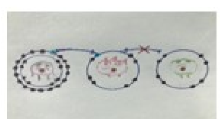


Damaging healthy cell



Become sick

Antioxidant donates electron to FR and stop FR chain reaction



Healthy person remains healthy

In conclusion, a balance between free radicals and antioxidants is necessary for proper physiological function. Therefore, we must maintain a proper balance between free radicals' generation and antioxidants defenses in our body system to prevent oxidative damage. A large part of that balance is a proper diet and nutrient doses, including regular moderate exercising.

Cancer and anticancer

Fig. 1. A Symbol of cancer and anticancer

Normally, human body cells grow and divide to form new cells as they need them, but cancer is a disease caused when cells begin to divide without stopping and spreading into surrounding tissues. This is a disease caused by change or damage to DNA (deoxyribonucleic acid is the building block of life). Mostly, these diseasesare cases due to environmental risk factors. Many of these factors are controllable lifestyle choices. On the other hand, there are also anti-risk factors which protect our health from risk factors.

How can we control risk factors and prevent diseases?

Fig. 2 **Fig. 3** **Fig. 4**

Healthy person (Fig. 2) Become an unhealthyand sick person (Fig. 3) → ? (Riskfactors) Become a healthyperson again (Fig. 4) → ? (Anti-riskfactors)

Fig. 5 **Fig. 6** **Fig. 7** **Fig. 8**

Healthy people(Figs. 5 and 6) Remain healthy (Figs. 7 and 8)

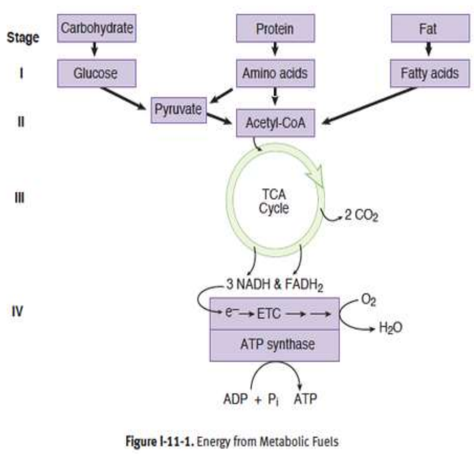
→ ? (Anti-risk factors with rightbalance between risk and anti-risk factors includingexercising)

Therefore, it is important and essential to know whatthe risk factors and anti-risk factors areto protect our health and remain healthy. Free radicals are risk factors that cause cancer and other diseases, but antioxidants are good or anti-risk factors that work as anticancer and protect our health from diseases like cancer. Now, we must know which agents are responsible for creating free radicals (FRs) and how they damage our cells and cause cancer and other diseases. Also, we need to know which sources are for antioxidants and how these work against FRs and protect our health from diseases.

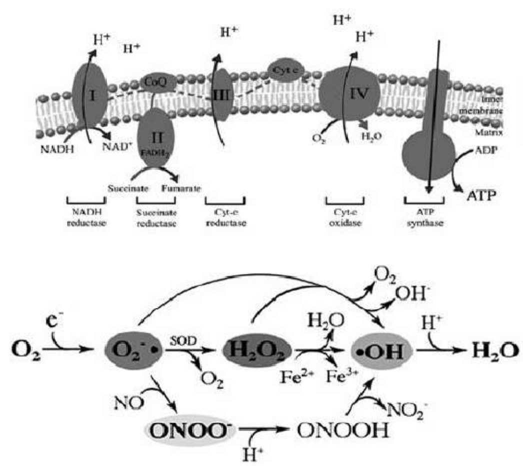
Cancer (Free Radical) and anticancer (Antioxidant)

Fig. 9. A symbol of free radicals and antioxidants working together

Free radicals (FRs) are produced in our body's cells during food oxidative metabolism (Figs. 10a, b). Metabolism is the sum of chemical reactions that occur within each cell to supply energy for important cellular processes. That means, the process through which humans/organisms use oxygen to break down food molecules to extract chemical energy (ATP, Adenosine triphosphate is the source of energy at the cellular level) for cell processes is known as oxidative metabolism, or cellular respiration. Also, there are a lot of internal and external sources of free radicals.



(a)



(b)

Figs. 10a, b. Free radicals (FRs) are produced/created during food oxidative metabolism for ATP formation by the mitochondria in our body’s cells

The FRs are the risk factors that can lead to cancer and other diseases, whereas antioxidants can reduce excess free radicals (oxidative stress) and protect us from cancer, as well as from other diseases.

The action mechanisms of free radicals and antioxidants are following:

1. Free radicals have an unpaired electron in their outer orbit (Fig. 11), and molecules in this state get veryhungry for that missing electron (Fig. 12).

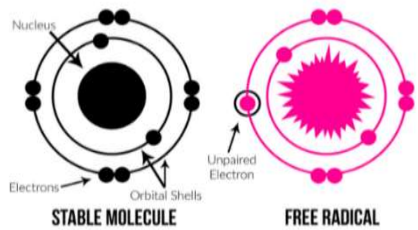


Fig. 11. Free radicals have an unpaired electron in their outer orbit

Fig. 12. For example, FR is like a hungry person who becomes very eager to get food

2. Free radicals attack normal cells for electrons so that they can become stable but produce newer FRs (Fig. 13). It reacts like a chain reaction (Fig. 13), and more free radicals damage more and more healthy cells (Figs. 14a, b).

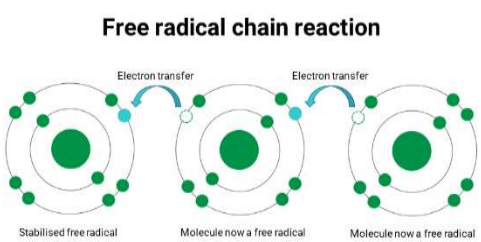


Fig. 13. Free radical attacks normal cell for electron

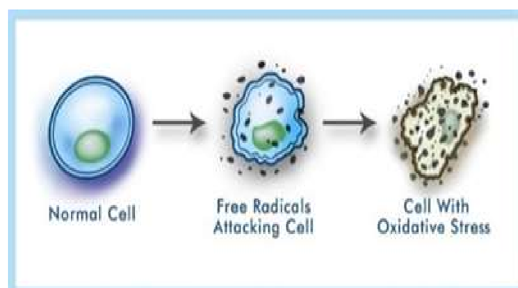


Fig. 14a. FRs damage healthy cell

Fig. 14b. For example, FRs damage healthy cell like a hungry person who becomes very eager to get and eat all the food

3. Antioxidants donate electrons to the free radicals (Fig. 15), making the FRs become stable and stopping FRs production and prevent free radical damage (Fig. 16). However, antioxidants would not become a free radical because they have a lot of electrons.

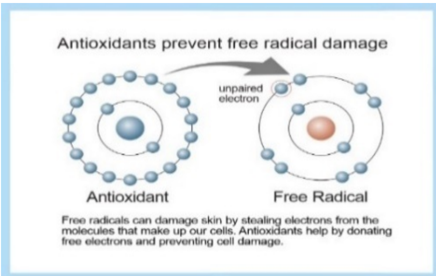


Fig. 15. Antioxidants donate electron to the free radical

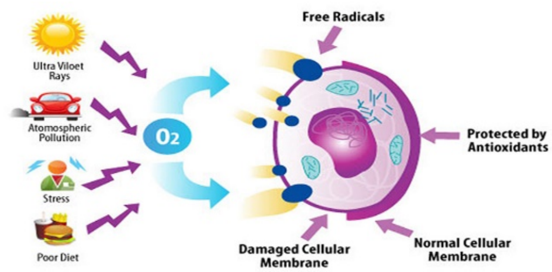


Fig. 16. Antioxidants protect cellular damage from FRs

For example, hungry people become full (Fig. 17) when rich people provide food to them (Figs. 17, 18). On the other hand, rich people would not become hungry people after donating food to the hungry people because rich people have a lot of food.

Fig. 17

Fig. 18

Figs. 17, 18. Hungry people become full (FRs become stable) when rich people (antioxidants) provide food (electrons) to them (FRs)

Sources of Free Radicals: Food metabolism, infection and inflammation, mental stress, ischemia, cancer, aging, air pollution, cigarette smoke, industrial solvents, radiation, heavy metals, etc.

Sources of Antioxidants: Beta carotene, vitamin A, vitamin E, vitamin C, carotenoids, selenium, manganese, zinc, flavonoids, omega-3, omega-6 fatty acids, etc. Bright colors rich diet/foods protect the body from cellular damage caused by free radicals and thus help the body function properly. Good sources of foods that contain rich antioxidants are cabbage, asparagus, spinach, tomatoes, broccoli, kale, collard greens, cucumbers, bell peppers, onions, carrots, lemon, raspberries, apricot, watermelon, lettuce, sweet potatoes, green tea, cantaloupe, winter squash, lobster, crab, shrimp, seaweed, salmon, etc.

To become healthy-"Maintain A Right Balance"

Fig. 19. A symbol of right balance

As with anything in life, we need to maintain a proper balance.

Fig. 20

Fig. 21

Fig. 22

Healthy person (Fig. 20)

→Free radicals make an unhealthy and sick person (Fig. 21)

→Antioxidants help to become a healthyperson again (Fig. 22)

Fig. 23

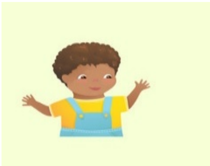


Fig. 24

Fig. 25

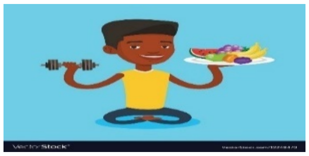


Fig. 26

Healthy people (Figs. 23, 24)

Remain healthy (Figs. 25, 26)

Antioxidants (right amount to maintain a proper balance between FRs generation and antioxidants defenses) andmoderate exercise

Always, maintain a proper balance/right balance between FRs generation and antioxidants defenses (Fig. 27).

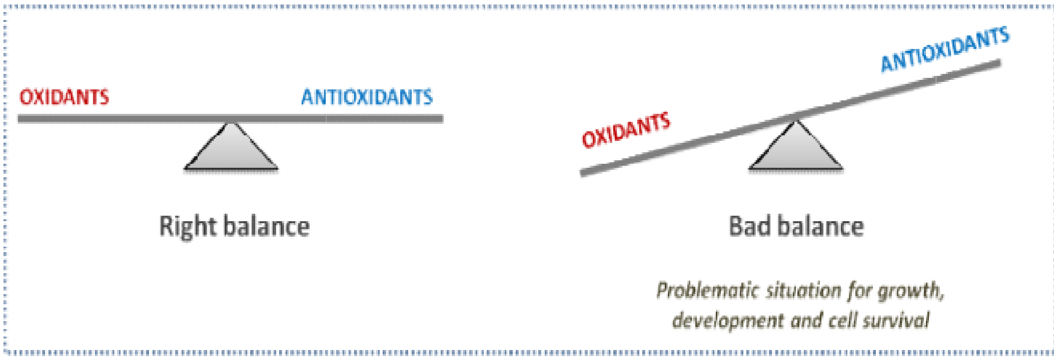


Fig. 27. A right balance between Free Radicals and Antioxidants

Oxidation is a chemical reaction that can produce free radicals, leading to chain reactions, and generate more and more free radicals that may damage more and more healthy cells. They attack macromolecules (including DNA, protein, lipid, carbohydrate, etc.) for electrons to become stable and that causes cellular/tissue damage. Free radicals may play a role in cancers (breast cancer, prostate cancer, lungs cancer, gastric cancer, colorectal cancer, etc.), inflammations, diabetes, heart disease, brain diseases, lung diseases, kidney diseases, eye diseases, joints pain, stroke, Alzheimer's, Parkinson's, and other age-related diseases and disorders. However, an antioxidant is a molecule that inhibits the oxidation of other molecules like free radicals by donating electrons, in which they become stable, and stop more free radicals' production and prevents free radical damage.

A balance between free radicals and antioxidants (Fig. 27) is very important for proper physiological function. The overwhelming amount of free radicals in the body increases the likelihood of damage to healthy cells, and this resulting damage is called oxidative stress. Therefore, we must maintain a proper balance between free radicals' generation and antioxidants defenses in our body system to prevent oxidative damage. The main part of that balance is a proper diet and proper nutrient dosages, including regular moderate exercising.

Formation of free radicals (FRs) in our body's cells

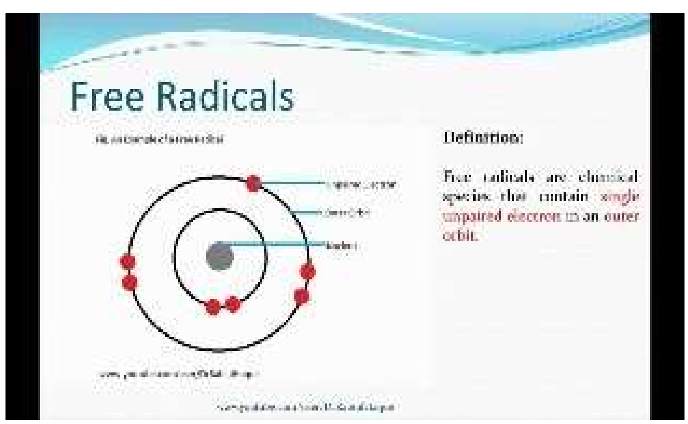


Fig. 28. A symbol of free radical

The mechanism for formation of FRs such as "Superoxide Radical ($O_2^{\bullet -}$) and Hydroxyl Radical ($OH^{\bullet}$)" in our body's cells is shown in Fig. 29.

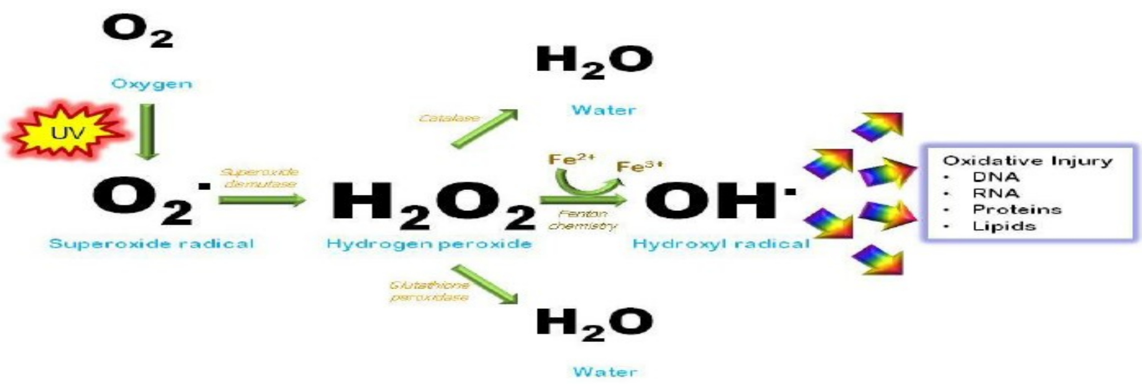


Fig. 29. Mechanism for formation of FRs in our body's cells

Free radicals have an unpaired electron in their outer orbit, and molecules in this state get veryhungry for that missing electron. Free radicals attack normal cells for electrons so that they can become stable but damage the normal cells and create more FRs. For example, FRs damage or break a chemical bond of DNA (DNA is the building block of life) and produce more FRs (Fig. 30).

Fig. 30. FRs damage DNA (Deoxyribonucleic acid)

Free radical (FR) formation is a chain reaction

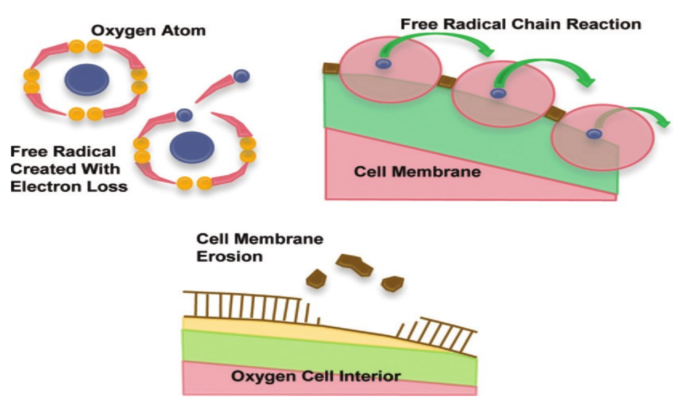


Fig. 31. A symbol of FR formation is a chain reaction

Free radicals are produced in our body's cells as a byproduct of food metabolism and by exposure to toxins in the environment. FRs serve both harmful (induce cancer and other diseases) and beneficial purposes (keep our body's immune system active).

Free radicals are defined as unstable atoms or compounds in the body, but their reactivity is very strong. They are unstable because they have an unpaired electron in their outer orbit (Fig. 32)[1-5]. Molecules in this state get very hungry to replace that missing electron, and they attack a normal cell for the electron to become stable. When this happens, it can result in a new free radical, which means it's a chain reaction (Fig. 33). Through this chain reaction, there is a production of more and more FRs which leads to damage of more and more healthy cells in the body.

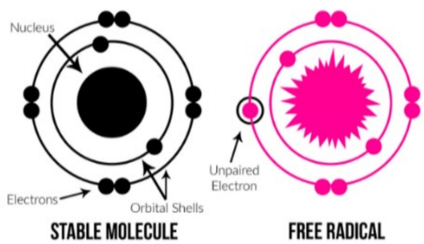


Fig. 32. FRhas an unpaired electronin its outer orbit

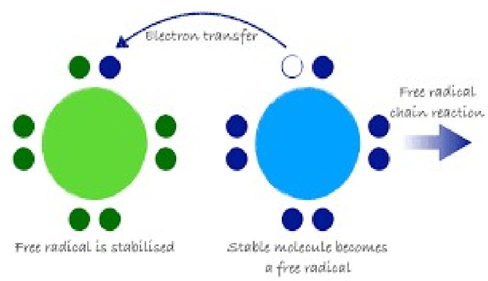


Fig. 33. FR attacks healthy cell for the electron to become stable, resulting in a chain reaction.

Free radicals collect their missing electron from molecules in the cells via the breakage of a chemical bond (damage parts of cells such as cell membranes, proteins, lipid, DNA, carbohydrate, and by stealing their electrons through a process called oxidation), and each fragment keeps one electron (unpaired electron i.e., form more new free radicals). They are a natural byproduct of our body's cells metabolism when they use oxygen to produce chemical energy (ATP) for proper cell function. Internally, free radicals are created during ATP (adenosine triphosphate) production by the mitochondria of the cell (Fig. 34)[3,6].

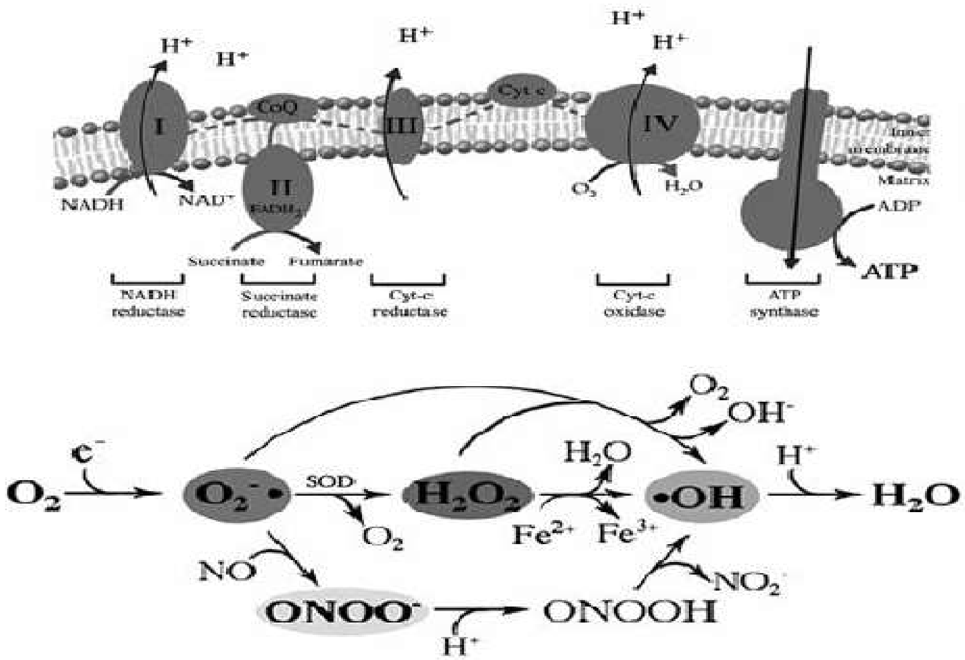


Fig. 34. Free radicals are created during ATP production by the mitochondria in our body's cells

Internally and externally generated sources of FRs

Fig. 35. A symbol of externally generated sources of free radicals

There are internally generated (endogenous) sources and externally generated (exogenous) sources of free radicals[4,6,7] (Table 1).

Table 1. Internally generated (endogenous) and externally generated (exogenous) sources of FRs

Internally generated sources of Free radicals[8]	**Externally generated sources of Free radicals[9]**
Mitochondria (food metabolism)	Air[10] and water pollution (environmental pollutants)
Immune cell activation	Cigarette smoke[11,12], alcohol[13]
Inflammation	Food and food additives, poor diet[14]
Mental stress	Heavy[15] or transition metals (Cd, Hg, Pb, Fe, As)
Excessive exercise	Industrial solvents[16]

Ischemia	Cooking[17] (smoked meat, used oil, fat)
Infection	Medications[18]
Cancer	Pesticides, chlorine in water[19-21]
Aging, etc.	Radiation, Sun light, UV Light, X-rays, ozone, etc[22,23]

There are many other factors that contribute to generating free radicals, for example, too much bad foods, too little or a lot of oxygen, synthetic drugs, vigorous exercise (the faster wet breath, the faster and more FRs that we produce!), and a whole bunch of other causes.

The good news is that our body has the power to easily neutralize internal sources of free radicals, but the bad news is that we have more external sources of free radicals than our body can manage!

Different form of FRs is generated from different sources

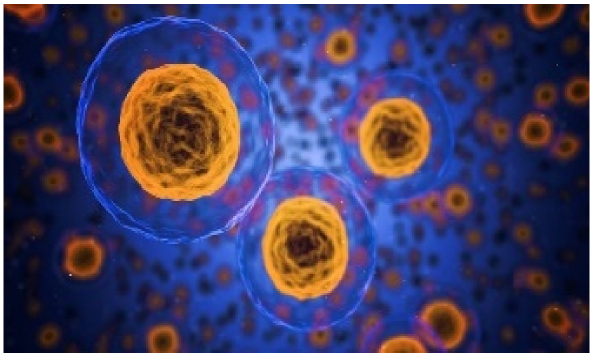


Fig. 36. A symbol of formation of free radicals

Free radicals such as reactive oxygen species (ROS) and reactive nitrogen species (RNS) are generated by the body's various endogenous systems, meaning they are exposed to different physiochemical conditions or pathological states. ROS and RNS can occur in the cells in two ways: enzymatic and non-enzymatic reactions. The important reactive free radicals in many disease states are hydroxyl radical, superoxide anion radical, oxygen singlet, hydrogen peroxide, hypochlorite, nitric oxide radical, and peroxynitrite radical (Table 2). Superoxide radical ($O2\bullet^-$), the most reactive free radical in vivo, and hydroxyl radical ($OH^\bullet$) are formed by the reaction of O_2 with H_2O_2 in the presence of Fe^{2+} or Cu^+ (catalyst) during metabolism[3] (Figs. 29, 34).

Table 2. The sources which are generated different form of free radicals

Sources	Free Radicals Form (examples)
Mitochondria (food metabolism)	Hydroxyl radical ($OH^\bullet$), Superoxide radical ($O_2\bullet^-$)

Air Pollution	Hydroxyl radical ($OH^{\bullet}$), Nitrogen dioxide ($NO_2^{\bullet}$),
White blood cell inflammation	Nitric oxide radical ($NO^{\bullet}$)
UV Light	Hydroxyl radical ($OH^{\bullet}$)
Radiation	Hydroxyl radical ($OH^{\bullet}$)
Smoking, Cigarette smoke	Hydroxyl radical ($OH^{\bullet}$)
Alcohol	Alcohol promotes the generation of ROS and oxidative stress
Diets high in carbohydrates, sugar, and processed foods	Cause oxidative stress

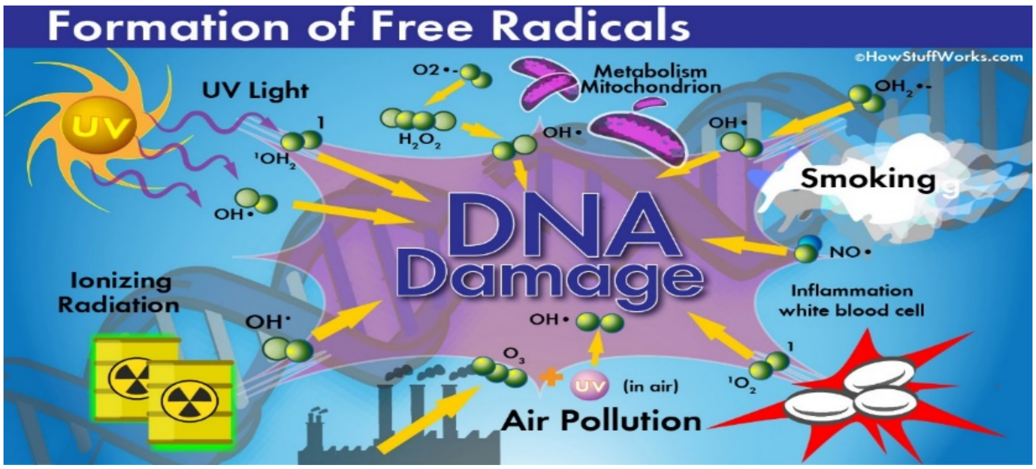


Fig. 37. A symbol of externally and internally generated sources of free radicals and damaged DNA

Cigarette smoke induced free radical formation

Fig. 38. A symbol to stop cigarette smoking

Tobacco smoke contains many toxic, carcinogenic and mutagenic chemicals, as well as stable and unstable free radicals and reactive oxygen species (ROS) in two different phases, one in the tar phase and one in the gas phase with the potential for biological oxidative damage[24].

The tar phase contains several relatively stable free radicals such as superoxide, hydrogen peroxide, and hydroxyl radicals(Fig. 39)[25].

The gas phase of cigarette smoke contains more reactive radicals than the tar-phase radicals[25]. These gas-phase radicals are produced in a steady state by the slow oxidation of NO to NO_2 in the air, which is much more reactive and then reacts with reactive species in smoke such as isoprene[25]. Nitrogen dioxide in smoke could react with hydrogen peroxide and produce $O_2^{\bullet -}$ (Superoxide radical) and $OH^{\bullet}$ (Hydroxyl radical) (Fig. 39)[25].

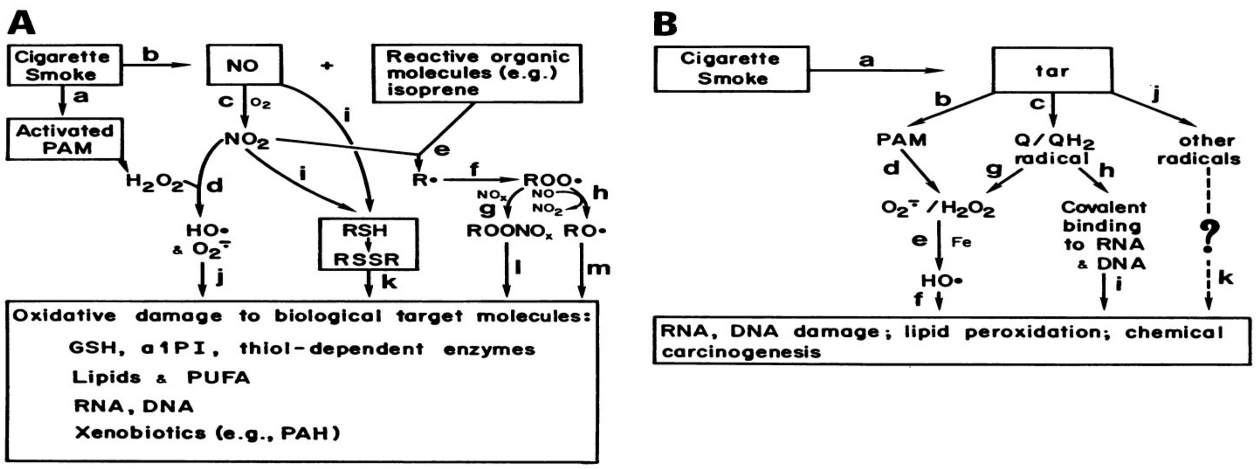


Fig. 39: Schemes summarizing[25] (A) the free radical chemistry of gas-phase cigarette smoke and possible biological consequences, (B) chemical reactions and possible biological consequences of the radicals associated with cigarette tar.

These reactive free radicals damage biological target molecules such as DNA, RNA, lipids, GSH (glutathione), thiol-dependent enzymes, etc[25]. These radicals are chemical carcinogenesis.

Tobacco smoking is responsible for approximately 30% of all cancer deaths in developed countries[26]. Smoking causes a greater number of deaths from cardiovascular, chronic obstructive pulmonary, and degenerative diseases. Ezzati, M., et al (2000)[27] reported that 4.8 million premature deaths worldwide were attributed to smokingof which 2.4 million people in developing and 2.43 million people in developed countries. These numbers could be increased to 10 million by 2030[28].

Arsenic (metal and metalloid) induced free radical (ROS, Reactive Oxygen Species) formations

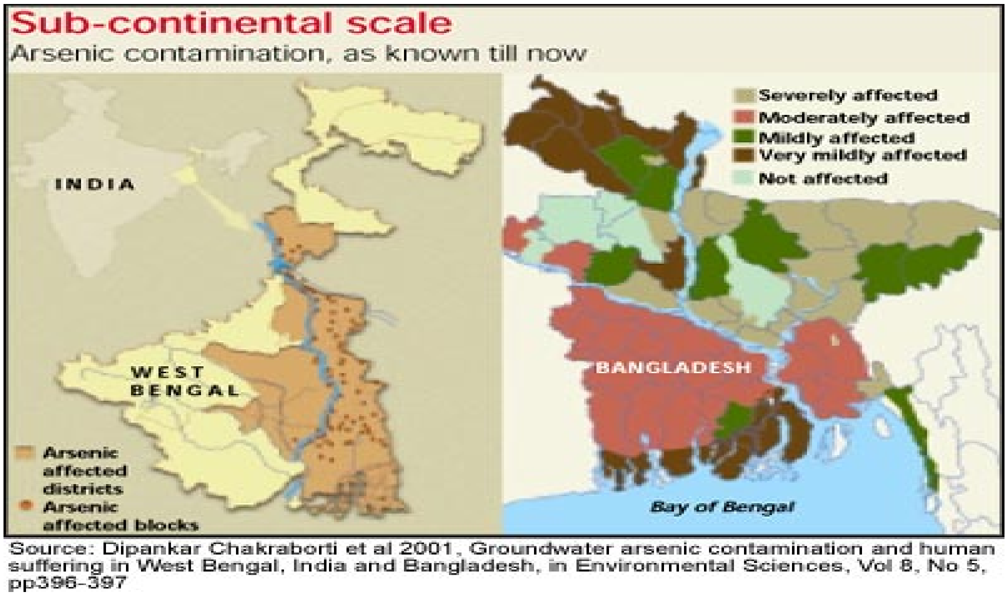


Fig. 40. Arsenic affected areas in Bangladesh and West Bengal-India

Arsenic (As) is a metal and metalloid. There are millions of people exposed/had been exposed to arsenic through their drinking water all over the world. However, the molecular mechanisms of its toxicity/carcinogenicity have remained an enigma, perhaps because As^{V}, arsenate, is biochemically transformed to at least five other arsenic-containing metabolites[29,30] (As^{III}, arsenite; MMA^{V}, monomethylarsonate; MMA^{III}, methylarsonous acid; DMA^{V}, dimethylarsinic acid; DMA^{III}, dimethylarsinous acid)(Fig. 41).

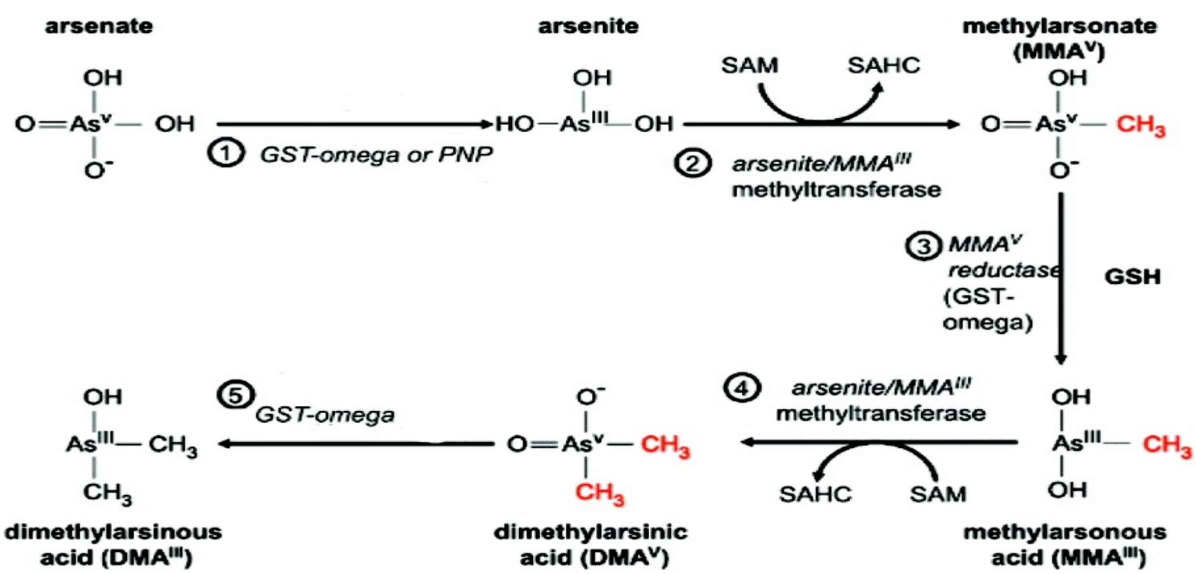


Fig. 41. Biotransformation of inorganic arsenic in human

However, reactive oxygen species (ROS) can be generated by arsenicals in our body's cells that play a role in inducing oxidative stress and mediated toxicity (Fig. 42).

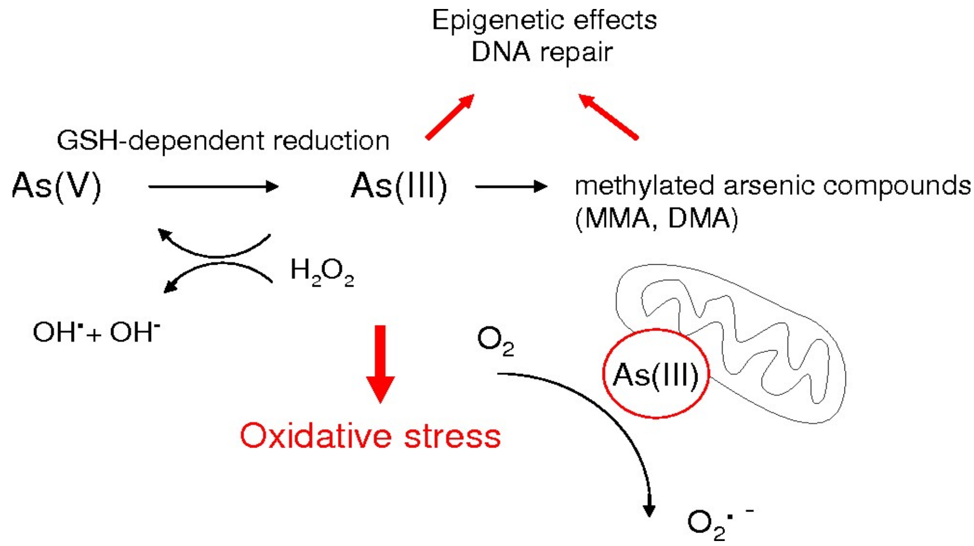


Fig. 42. ROS (Reactive Oxygen Species, free radicals) generated by arsenicals and its impact

There is evidence that arsenic induces DNA damage via the production of reactive oxygen species (ROS)[31,32]. GST-pi mightbe over expressed in the urinary bladder (Figs. 43a, b) to protect cells against arsenic-induced oxidative stress[33-35].

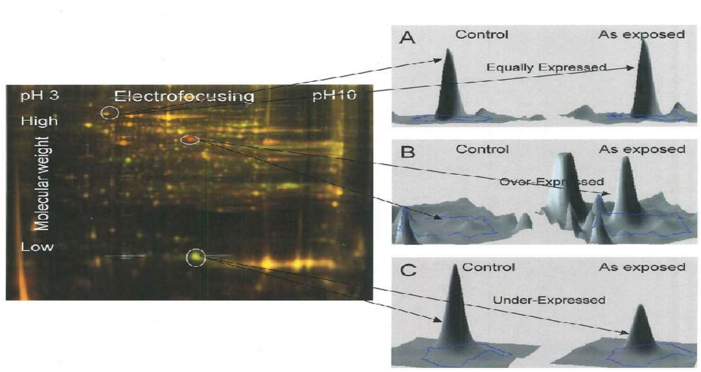


Fig. **43a**

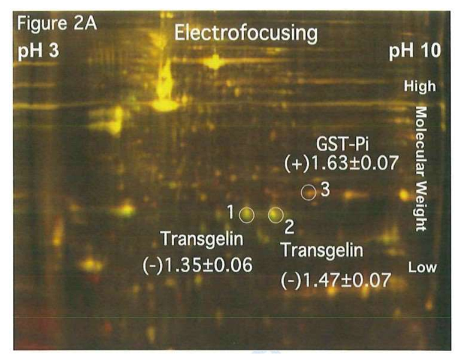


Fig. **43b**

Figs. 43. (a) Three-dimensional stimulation of equally-, over-, and under expressed protein spots in the tissue of a hamster that is exposed to sodium arsenite as compared to the sample of control hamster with the use ofDeCyder software (Yellow: Equally expressed; Red: Over expressed; Green: Under expressed), (b) GST-pi might be over expressed in the urinary bladder to protect cells against arsenic-induced oxidative stress.

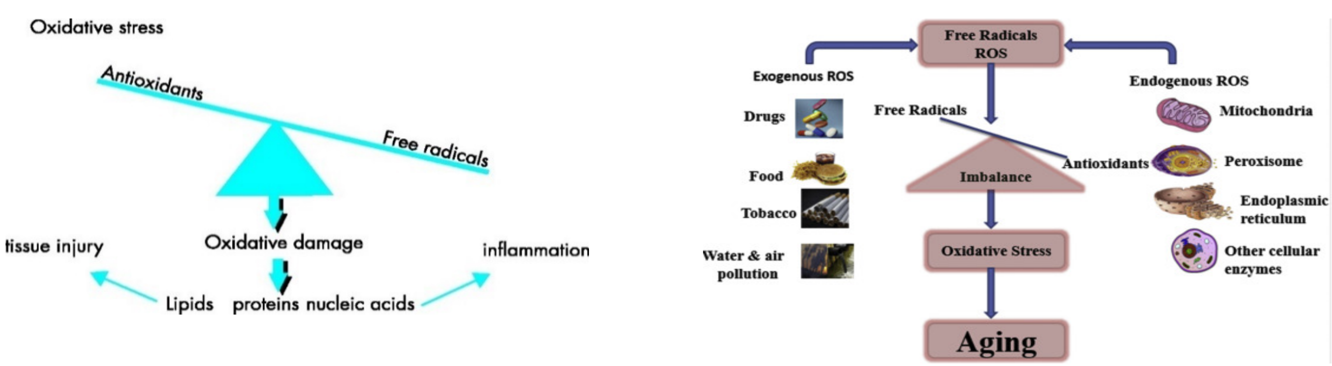
The presence of high concentrations of inorganic arsenic in drinking water is a major health problem in many parts of the world and results in an increased risk of cancer, circulatory diseases, and perhaps diabetes. Other complications such as liver enlargement, spleen enlargement, and fluid in the abdomen are seen in severe cases. Squamous cell carcinoma, basal cell carcinoma, Bowen disease, and carcinoma affecting the lung, uterus, bladder, or other sites are often seen in patients with advanced cases that have suffered for many years (Photographs 1)[36,37].

Photographs 1: A few examples of arsenic health impacts of the people in Bangladesh

Oxidative stress- induce diseases

Fig. 44. A symbol of oxidative Stress

Free radicals damage DNA and induce diseases:Free radicals could take electrons from DNA molecules, proteins, fats, carbohydrates, and other molecules, damaging and turning them into new free radicals. In this process, free radical chain reactions damage the entire cell, then their neighbors, and so on. The overwhelming radicals in the body contribute to a greater likelihood of damage to healthy cells. This resulting damage is called oxidative stress and occurs when there are too many free radicals as compared to antioxidants[1,38] (Figs. 45-49). Elevated ROS levels can cause severe damage to the cells, and this damage causes a loss for their ability to divide and multiply. Semba, R. D., et al (2007)[39] reported that oxidative stress damage to proteins is associated with greater mortality in older women. They found that the elevated serum protein carbonyl concentrationswere associated with greater risk of death in older women living in a community, and protein carbonyls are the most studied marker of protein oxidation[40].



Figs. 45 & 46. Oxidative stress due to overabundance of FRs comparing to antioxidants and its impacts

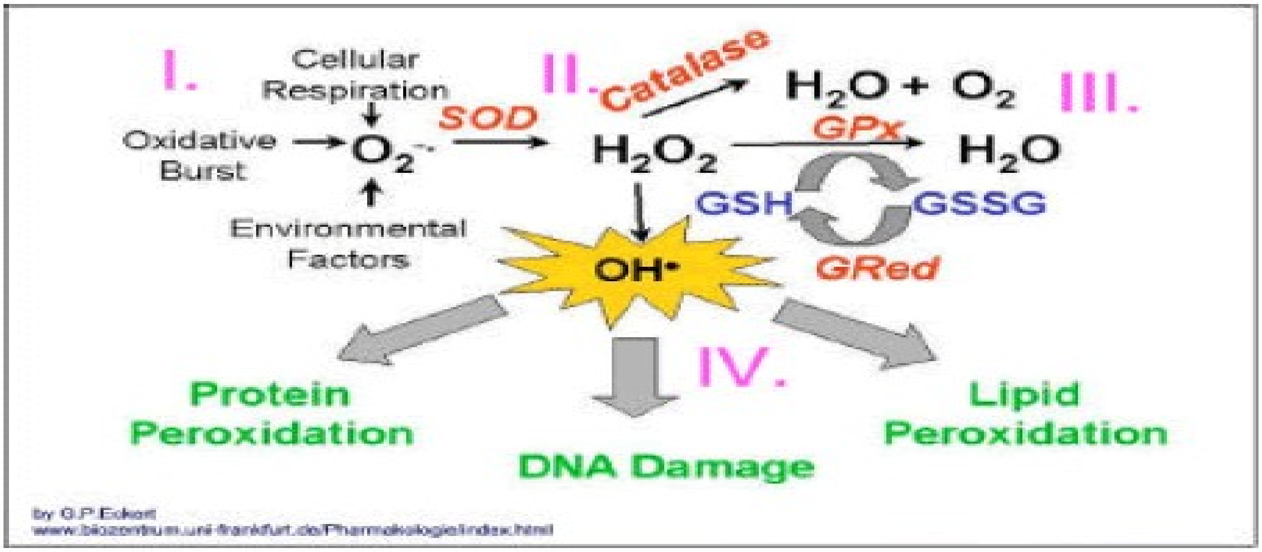


Fig. 47. Impact of Oxidative stress (Damaging DNA, lipid, and protein)

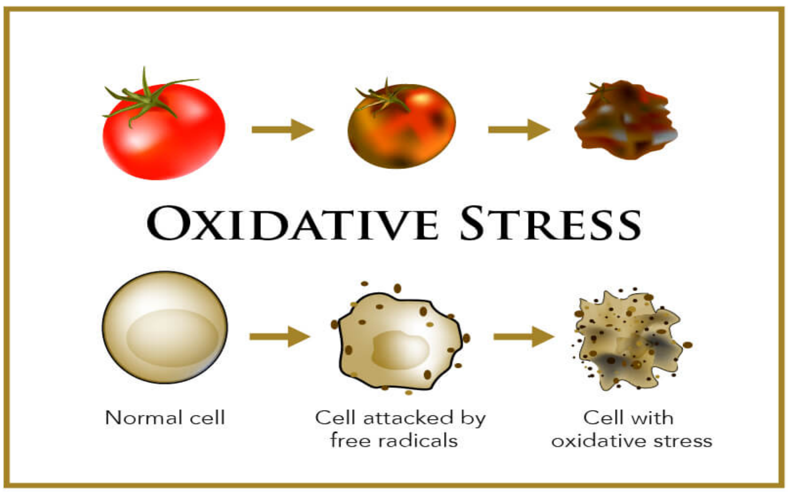


Fig. 48. Impact of Oxidative stress (symbol of cell damage)

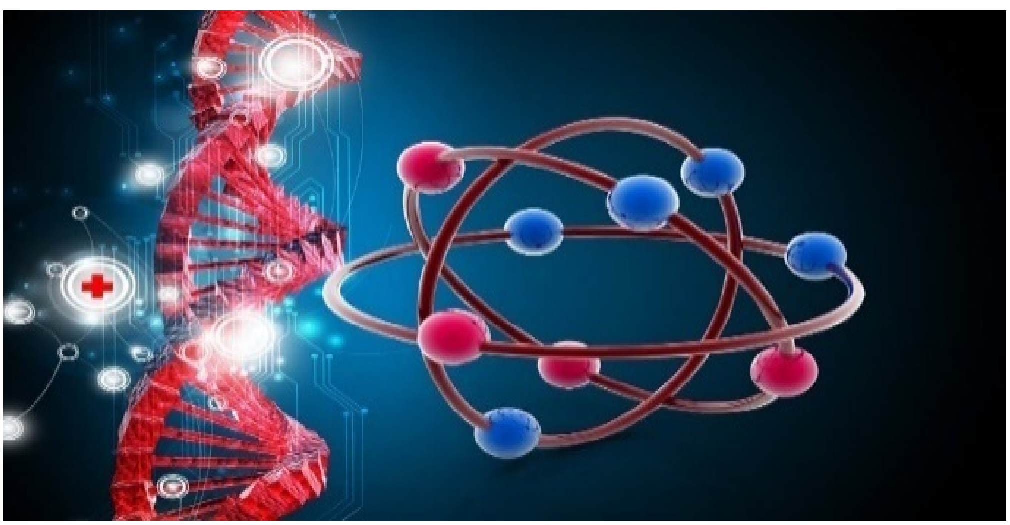


Fig. 49. Impact of Oxidative stress (symbol of DNA damage)

For example, oxidative stress (overabundance of free radicals)-induced the following diseases in humans[3]:

Lungs	Asthma, Chronic bronchitis
Kidneys	Glomerulonephritis, Chronic renal failure
Multi-organs	Cancers, Diabetes, Inflammation, Infection, Aging
Heart-Vessels	Cardiomyopathy, Heart failure, Arteriosclerosis, Hypertension, Ischemia
Brain	Alzheimer's, Parkinson's, Stroke, Memory loss, Depression
Eyes	Cataract, Retinal diseases
Fetus	Preeclampsia, IU growth restriction
Joints	Arthritis, Rheumatism

Avoid high temperature cooking

Fig. 50. A symbol of high temperature cooking

Foods that increase Free Radicals[4]:

Fats and Oils

When fats or oils are heated to high temperatures, they can become oxidized and produce free radicals. Unsaturated fats become more oxidized than saturated fats. If cooking fats are reused, they become more oxidized and produce even more free radicals.

Cooked and Processed Meats

Meat fats become oxidized when cooked at high temperatures. The iron found in meat can also become oxidized. Preservatives used in processed meats may also create free radicals.

Traditional Holiday Meals

While traditional holiday meals are laden with salt, fat, and sugar, many foods that we eat regularly, such as sweets and sodas, can also spike blood glucose and insulin levels. They also can increase the amount of free radicals, or molecules with unpaired electrons, in the body, which can do serious cellular damage.

Alcohol Risks

Alcohol intake increases the risk of cancer by creating free radicals in our body, but moderate alcohol intake may have some heart health benefits.

Overeating

Our mitochondria release/produce more activated oxygen when overeating during energy consumption and generating higher levels of free radicals.

Exhaustive exercise

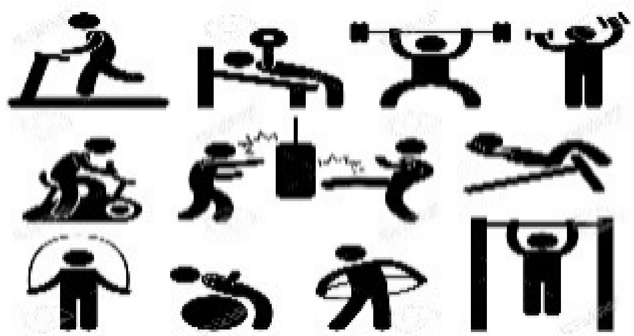


Fig. 51. A symbol of exhaustive exercise

Moderate exercise is a healthy practice, but exhaustive exercise generates free radicals (Fig. 52). This can be confirmed by increases in lipid peroxidation, glutathione oxidation, oxidative protein damage, and cytosolic enzymes level in blood plasma which are increased after exhaustive exercise[41].

Exercise speeds up the rate of metabolism at which we burn more calories and lose weight. In the process of burning up calories, exercise does indeed generate more free radicals, but it also improves the body's control mechanisms[42].

Moderate exercise produces healthy amounts of oxidative stress, and most researchers call it an antioxidant.It is scientifically proven that regular exercise protects our health against heart disease, stroke, hypertension, diabetes, obesity, and even malignancies such as colon cancer, breast cancer, and possibly prostate cancer. The concern is that exhaustive exercise may have the opposite effect[43].

However, at low or moderate levels, free radicals are a key component in the function of the immune system. For example, small amounts of free radicals even act as a defense mechanism against invading microbes[3]. However, we must control or stop excess production of free radicals in our body system by controlling our food habits and lifestyles.

The theory of Oxygen-Free Radicals has been known for about fifty years[4]. However, only within the last few decades, there has been an explosive discovery of their roles in the development of diseases and of the health protective effects of antioxidants[3].

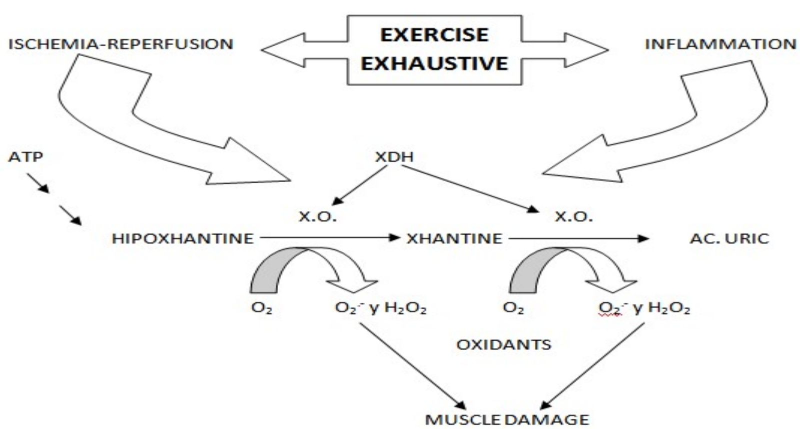


Fig. 52. Exhaustive exercise generates free radicals

Defense mechanism is the key role of FRs

Fig. 53. A symbol of defense mechanism

At low or moderate levels, free radicals are a key component in the function of the immune system. For example, healthy or small amounts of free radicals act as a defense mechanism against invading micro-organisms, and FRs also play a role in cell signaling to start or stop making various proteins. However, we must control or stop excess production of free radicals in our body system by controlling our food habits and lifestyles.

Macrophages, neutrophils, and monocytes produce free radicals, but they use these free radicals as a part of their defense mechanism. Also, free radicals generated by them are used to kill foreign micro-organisms.

What are antioxidants, and how do they work?

Fig. 54. The sources of antioxidants

Antioxidants are molecules that donate electrons to free radicals (Fig. 55) without becoming free radicals and destabilize themselves in the process that protects cells from the damage (Fig. 56) caused by free radicals[43]. In this way, they are stopping that negative chain reaction.

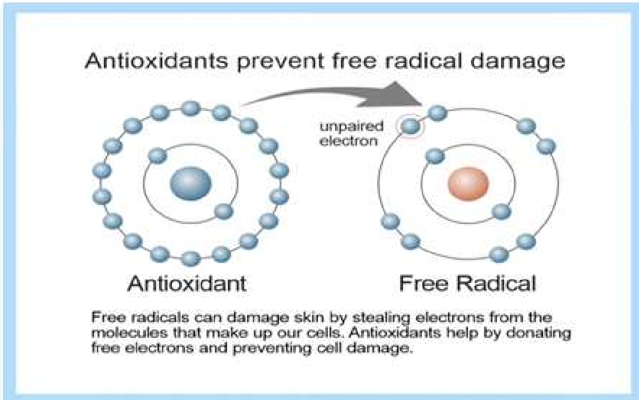


Fig. 55. Antioxidant donates electrons to the FR without becoming a free radical, itself.

Fig. 56. Antioxidants protect cellular damage from FRsby stopping the negative chain reaction.

Antioxidants counteract free radicals in two ways[1,44]:

1. Antioxidants can safely interact with free radicals, stabilizing or neutralizing the volatile compounds and ending the harmful chain reaction.

2. It can reduce oxidative stress by stopping the formation of new free radicals before they can initiate their chain reaction.

Our bodies naturally produce a variety of antioxidants, such as alpha lipoic, glutathione, flavonoids, bilirubin acid, etc., to neutralize excessive free radicals. This is why antioxidants are commonly seen as promoting immunity and acting as a defense against many chronic diseases. However, the largest source of antioxidants comes from our diet, including beta-carotene, vitamin A, vitamin E, vitamin C, carotenoids (lycopene, lutein, zeaxanthin), selenium, manganese, zinc, flavonoids, omega-3, and omega-6 fatty acids, spices, etc[1].

Sources of Antioxidants[45]

Fig. 57. A symbol of the source of antioxidant

Figs. 58-61. The sources of antioxidants

Bright colors rich diet/foods protect the body from cellular damage caused by free radicals and thus help the body function properly[45]. Good sources of foods that contain rich antioxidants are cabbage, asparagus, spinach, tomatoes, broccoli, kale, collard greens, cucumbers, bell peppers, onions, carrots, lemon, raspberries, apricot, watermelon, cherries, artichokes, orange, cranberries, lentils, kidney beans, corn, grapefruit, peaches, pomegranate, raisins, blueberries, cranberries, figs, prunes, pomegranates, red capsicum, kale, spinach, guava fruit, dark chocolate, turmeric, clove, ginger, cinnamon, cumin, pecans, green tea, etc. Beta carotene rich foods, including dark leafy greens (such as kale and spinach), romaine lettuce, sweet potatoes, carrots, broccoli, butternut squash, cantaloupe, red and yellow peppers, apricots, podded peas, coriander, Mustard Greens, etc.

Vitamin A rich foods, includingcarrots, tuna, butternut squash, sweet potato, spinach, cantaloupe, lettuce, red bell peppers, pink grapefruit, broccoli, etc.

Vitamin E[46] rich foods, includingsunflower seeds, almonds, avocados, spinach, butternut squash, mango, kiwifruit, broccoli, trout, olive oil, shrimp, etc.

Vitamin C rich foods, includinglemon,grapes fruits, pomegranates,oranges, guavas, bell peppers, kiwifruit, strawberries, papayas, broccoli, tomatoes, kale, snow peas, etc.

Carotenoids (lycopene, lutein, zeaxanthin) rich foods, includingkale, spinach, broccoli, lettuce, green beans, corn, fruits, eggs, fish, avocado, zucchini, cucumber, asparagus, etc.

Selenium[46] rich foods, including Brazil nuts, whole wheat bread, chia seeds, sunflower seeds, tuna fish, shrimp, salmon, brown rice, oats, mustard seeds, etc.

Manganese rich foods, including sweet potatoes, pineapples, oats, cloves, whole grains, clams, oysters, mussels, nuts, soybeans and other legumes, brown rice**,** spinach, coffee, tea, and many spices, such as black pepper, etc.

Zinc rich foods, including meats, shellfish, lentils, beans, seeds, nuts, dairy products, eggs, whole grains, oysters, carb, chickpeas, Greek yogurt, cashews, etc.

Flavonoids: Flavonoids are present in red wine, onions, eggplant, lettuce, parsley, pears, berries, cherries, legumes, soybeans, tofu, miso, etc.

Omega-3 rich foods, includingfish such as salmon, tuna, mackerel, chia seeds, flax seeds, walnuts, soybean oil, canola oil, cod liver oil, herring, oysters, sardines, etc.

Omega-6 fatty acids are rich in foods, including soybeans, corn, safflower and sunflower oils, nuts and seeds, meat, poultry, fish, and eggs, etc.

Spices can reduce oxidative stress: such as ginger, turmeric, clove, cinnamon, grape seed extract and rosemary.

β-carotene: The richest sources of beta-carotene are yellow, orange, and green leafy (the more intense the color, the more beta-carotene it has) fruits and vegetables (such as carrots, spinach, lettuce, tomatoes, sweet potatoes, broccoli, cantaloupe, and winter squash).

Antioxidants in Foods

Antioxidant	Sources
Vitamin E	Sunflower seeds, almonds, peanut butter, wheat germ oil, avocados
Vitamin A	Carrots, sweet potatoes, liver, pumpkin, turnip greens
Vitamin C	Kiwis, sweet peppers, peaches, broccoli, citrus fruit
Cryptoxanthin	Butternut squash, tangerines, papaya, plums, corn
Selenium	Mixed nuts, turkey, wheat, tuna, wheat germ
Astaxanthin	Lobster, crab, shrimp, seaweed, salmon
Anthocyanin	Eggplant, blueberries, raspberries, blackberries, red cabbage
Lycopene	Tomatoes, guavas, watermelon, pink grapefruit, asparagus
Lutein	Spinach, kale, mustard green, swiss chard, green peas
Catechins	Dark chocolate, green tea, black tea, red wine, black grapes,
Quercetin	Onions, apples, parsley, olive oil, dark cherries

Table 3. The sources of antioxidants in foods

It is important to note that carotenoids are among the strongest antioxidants. These compounds are highly active against both ROSs and FRs. Comparing astaxanthin, β-carotene, and lycopene with other antioxidants (e.g., vitamin C and E), these compounds have higher antioxidant activity, e.g., against singlet oxygen. On the other hand, astaxanthin is a 54-, 14- and a 65-times stronger antioxidant compared to β-carotene, vitamin E, and vitamin C, respectively[47].

Antioxidants: Key Notes

Fig. 62. The sources of antioxidants

Antioxidants: Key Points[48]

- Vegetables and fruits are rich sources of antioxidants. There is good evidence that eating a diet that includes plenty of vegetables and fruits is healthy, and official U.S. Government policy urges people to eat more of these foods. Research has shown that people who eat more vegetables and fruits have lower risks of several disease developments; however, it is not clear whether these results are related to the number of antioxidants in vegetables and fruits, other components/factors of these foods, or other components/factors produced in our body in combination to these diets, including lifestyle choices.

- Rigorous scientific studies, involving more than 100,000 people combined, have tested whether antioxidant supplements can help to prevent chronic diseases, such as cardiovascular diseases, cancer, and cataracts. In most instances, antioxidants did not reduce the risks of developing these diseases.

- Concerns have not been raised about the safety of antioxidants in food. However, high-dose supplements of antioxidants may be linked to health risks in some cases. Supplementing with high doses of beta-carotene may increase the risk of lung cancer in smokers. Supplementing with high doses of vitamin E may increase risks of prostate cancer.

- Antioxidant supplements may interact with some medicines.

- Tell all your health care providers/doctors about any complementary and integrative health approaches you use. Give them a full picture of what you do to manage your health. This will help to ensure coordinated and safe care.

Are You Eating Too Many Antioxidants[49]?

Research does suggest that certain antioxidants may reduce risk for stroke, diabetes, cancer, etc., but it doesn't mean more antioxidants are better. Just like other natural, good-for-you substances (water, oxygen, iced tea, etc.), too much can be harmful. Here, we bust four of the biggest antioxidant myths:

Myth 1: When it comes to antioxidants, more is always better.

Truth: A 2015 study of Chinese people with high risk for liver cancer found that those with the highest intake of catechins—an antioxidant found in green tea—had even a greater risk for liver cancer.

Myth 2: Our bodies can utilize most of the antioxidants we eat.

Truth: Most phytochemicals (healthy plant compounds that are high in antioxidant activity) are super low in bioavailability, meaning they are difficult to absorb.

Myth 3: Food products with antioxidants are superior.

Truth: The Oxygen Radical Absorbance Capacity (ORAC) measures a food's ability to neutralize free radicals in a test tube—and antioxidants behave very differently in our body system than they do in test tubes.

Myth 4: All free radicals, which antioxidants fight, are evil and dangerous.

Truth: Diane McKay, PhD, a scientist at the Antioxidants Research Laboratory at Tufts University, says "If you increase antioxidant intake, you're also reducing free radicals to such a low level that you're limiting the body's normal adaptation to stress."

However, a study in India (Sharda, B., 2006)[50] shown that infants and children may undergo severe oxidative stress due to lower levels of antioxidant defenses. A rise in TAA (Total antioxidant activity) in antioxidant supplemented group of severely malnutrition children was higher with good outcome compared with the no-supplemented group, but it is better to be careful when supplementing antioxidants during nutritional management. This study has suggested that health benefits can be obtained by children with a reduced risk of disease from supplements of antioxidant nutrients.

The bottom line is that even if we don't know exactly why antioxidants are beneficial, experts agree we still need to get antioxidants from our diet (especially vitamins C and E, which are essential nutrients).

Preventing oxidative stress requires limiting our exposure to external sources of free radicalsand safely increasing our intake of antioxidants. A nutritious diet rich in fresh, whole foods is one of the best ways to increase our intake of antioxidants[1].

Summary

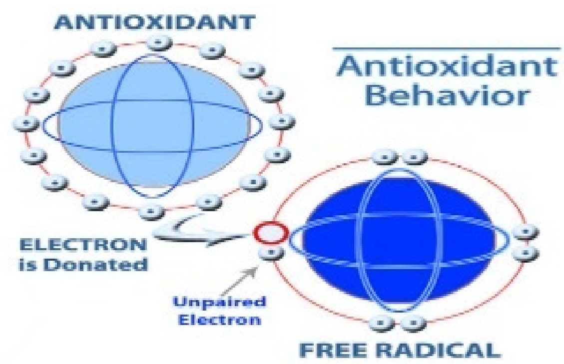


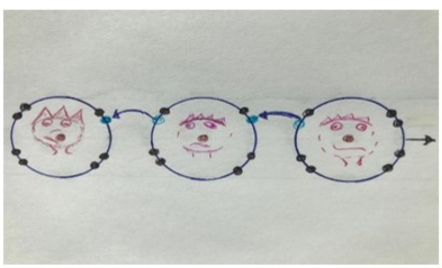
Fig. 63. FRs and antioxidants behavior

Mechanisms of free radicals produce, and antioxidants neutralize free radicals (Fig. 64a, b):

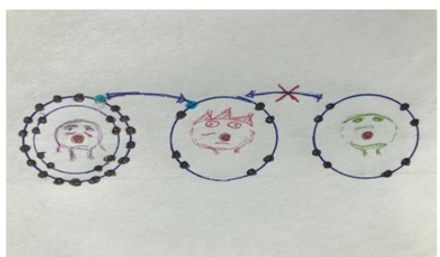
Electron transfer Electron transfer

Antioxidant donates electron to FR

Stop FR chain reaction



(a)



(b)

FR becomes stable by taking an electron from a healthy cell and creating a new FR

Healthy cell becomes aFR and creates another FR after becomingstableitself

Healthy cell becomes FRand takes electron fromanother healthy cell to becomestable, but also creates a new FR,and continuing this process

Antioxidant

Antioxidant donates electron to FR. Then, FR becomesstable and stop FR chain reaction i.e., prevent free radical damage

Healthy cell remainshealthy

Figs. 64. (a) Mechanisms of free radical chain reaction, (b) antioxidant neutralizes free radical and prevents FR damage by stopping chain reaction

Free radicals (FRs) take electrons from DNA molecules, proteins, fats, carbohydrates, cell membranes, and other molecules, damaging and turning them into new free radicals. In this process, free radical chain reactions damage the entire cell, then their neighbors, and so on.

Oxidative stress (overabundance of free radicals comparing with antioxidants) may play a role in diabetes, cancer, heart disease, brain diseases, lungs diseases, kidneys diseases, joint pains, stroke, and other diseases of aging.

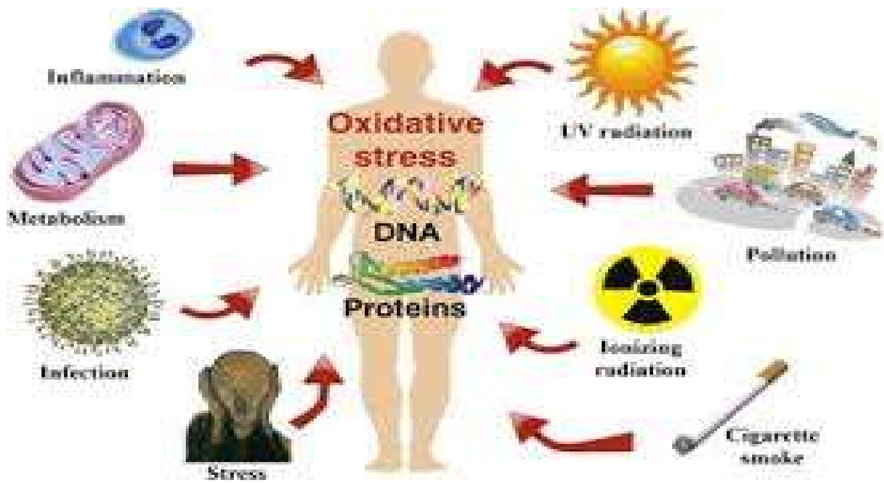


Fig 65. Oxidative stress due to overabundance of free radicals and damage to DNA, protein, etc.

However, at low or moderate levels, free radicals are a key component in the function of the immune system. For example, small amounts of free radicals can even act as a defense mechanism against invading microbes.

Antioxidants counteract free radicals in two ways[44]:

1. First, antioxidants can safely interact with free radicals, stabilizing or neutralizing the volatile compounds and ending the harmful chain reaction.

2. Another way is that they can reduce oxidative stress by stopping the formation of new free radicals before they can initiate their chain reaction.

To maintain a healthy life, we must continue a right balance between free radical generation and antioxidant defenses in our body system. With the help of a balanced diet and consistent exercise, our body can naturally fight off and leverage free radicals[38].

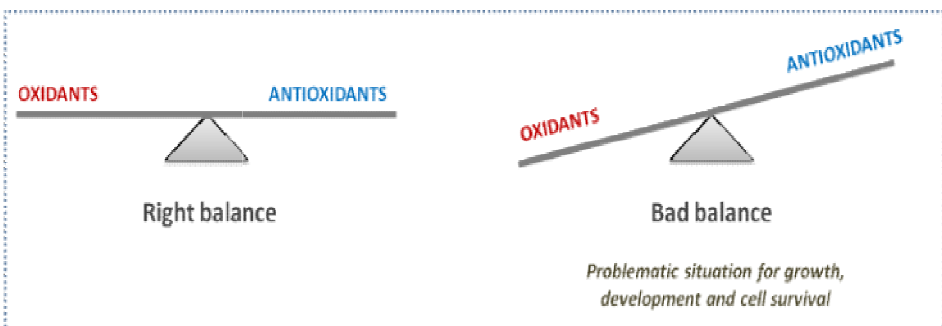


Fig. 66. Everyone must continue a right balance between free radical generation and antioxidant defenseto maintain a healthy lifestyle

Sources of Antioxidants:

Figs. 67-69. The sources of antioxidants

Balanced diet and consistent exercise are very important to maintain our good health:

Fig. 70

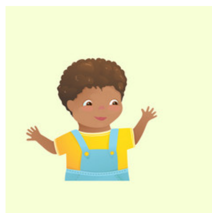


Fig. 71

Fig. 72

Fig. 73

Healthy People (Figs. 70 & 71) Remain Healthy (Figs. 72 & 73)

→ Antioxidants (right amount to maintain a proper balance between FRs generation and Antioxidants defenses) and moderate Exercise

Be Happy, Be Healthy, & Make the World Healthy!

Always maintain a proper balance between Free Radicals (oxidants) generation and Antioxidants defenses.

As with anything in life, we need to maintain a consistent balance.

N.B. This information is for educational purposes only, and you must always follow the advice of your physician for healthcare decisions.

Acknowledgement

Fig. 74. A symbol of Thank You

All information and images were collected from the internet/online, and authors are thankful to all of them for sharing their knowledge and information to improve our health. They/authors just collected, accumulated, and reorganized all this information, only for academic purposes and improving knowledge to maintain good health. Authors also would like to make known that "this information is not for business purposes, and they don't have any other interest except for helping people".

The authors tried to mention all the references and sources from where they collected the information in this review paper, but they apologize if there are any mistakes or didn't mention your references/sources here because it happened unwillingly.

Competing interests: The authors declare no competing interests.

Thank you,
Uttam Chowdhury, Shreya Chowdhury
Happy and Healthy (HAH)
happyhealthyukc@gmail.com

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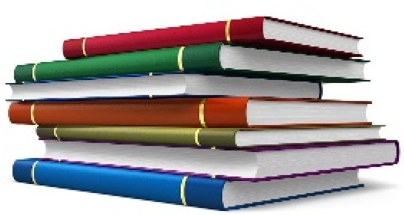

Fig. 75. A symbol of references

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Cancer and Anticancer:

Fig 1. nytimes.com, Fig 2. vectorstock.com, Fig 3. 123rf.com, Fig 4. vectorstock.com, Fig 5. depositphotos.com, Fig 6. vectorstock.com, Fig 7. vectorstock.com, Fig 8. vectorstock.com

Cancer (Free Radical) and Anticancer (Antioxidant):

Fig 9. pinterest.com, Fig. 10a. https://quizlet.com/733315915/kaplan-energy-metabolism-flash-cards,

Fig 10b. researchgate.net/figure/Mitochondrial-respiratory-chain-and-generation-of-free-radicals-Electron-transfer_fig1_6685486, Fig 11. mercordianimalcare.com, Fig 12. pnghut.com, Fig 13. formulabotanica.com, Fig 14a. globalbia.org, Fig 14b. depositphotos.com, Fig 15. medicaldetectivemd.com, Fig 16. vital-reaction.com, Fig 17. thehimalayantimes.com, Fig 18. pamplinmedia.com

To Be Healthy- "Maintain A Right Balance":

Fig 19. stock.adobe.com, Fig 20. vectorstock.com, Fig 21. 123rf.com, Fig 22. vectorstock.com, Fig 23. depositphotos.com, Fig 24. vectorstock.com, Fig 25. vectorstock.com, Fig 26. vectorstock.com, Fig 27. nutexa.com

Formation of Free Radicals (FRs) in our body's cells:

Fig 28. Youtube.com, Fig 29. Mdpi.com, Fig 30. Abolitionscience.org

FR formation is a chain reaction:

Fig 31. researchgate.com, Fig 32. mercordianimalcare.com, Fig 33. theconversation.com, Fig 34. researchgate.net/figure/Mitochondrial-respiratory-chain-and-generation-of-free-radicals-Electron-transfer_fig1_6685486

Internally and externally generated sources of FRs:

Fig 35. fuelrunning.com

Different form of FRs is generated from different sources:

Fig 36. wingsforlife.com, Fig 37. science.howstuffworks.com

Cigarette smoke induced free radicals' formation:

Fig 38. httpswww.dispatchlive.co.zanews2020-05-28-put-these-stats-in-your-pipe-and-smoke-them-ndz, Fig 39. Church, D. F., Pryor, W. A. Free-Radical chemistry of cigarette smoke and its toxicological implications. Environmental Health Perspectives, Vol. 64, pp. 111-126, 1985.

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Oxidative Stress- Induce Diseases:

Fig 44. orogoldingredients.com, Fig 45. sciencedirect.com, Fig 46. oem.bmj.com, Fig 47. scialert.net, Fig 48. orogoldingredients.com, Fig 49. newsnaturalusa.com

Avoid high temperature cooking:

Fig 50. askdrray.com

Exhaustive exercise:

Fig 51. 123rf.com, Fig 52. intechopen.com

Defense Mechanism is the key role of FRs:

Fig 53. siimland.com

What are antioxidants and how do they work?

Fig 54. bonvictor.blogspot.com, Fig 55. medicaldetectivemd.com, Fig 56. vital-reaction.com

Sources of Antioxidants:

Fig 57. eufic.org, Fig 58. marketmatters.com.au, Fig 59. belmarrahealth.com, Fig 60. foodrevolution.org, Fig 61. zovon.com, Table 3. livefertile.com

Antioxidants: Key Notes:

Fig 62. medicalnewstoday.com

Summary:

Fig 63. theartofmed.wordpress.com, Figs 64a&b. happyhealthyukc@gmail.com, Fig 65. onlinelibrary.wiley.com, Fig 66. nutexa.com, Fig 67. foodrevolution.org, Fig 68. zovon.com, Fig 69. pennmedicine.org, Fig 70. depositphotos.com, Fig 71. vectorstock.com, Fig 72. vectorstock.com, Fig 73. vectorstock.com

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Fig 74. happyfacechildren.com

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Fig 75. spineuniverse.com

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