Chapter 8

Free Radicals and the Skin

What exactly are **free radicals**? What do they have to do with skin care? This chapter provides an introduction to free radicals—how they are created and relate to the body. Although it can seem to be overwhelmingly difficult to understand, read on. Then, read it again for a clearer understanding of free radicals.

Early history

Molecular oxygen, as it is known today, has not always existed. About two billion years ago, oxygen was released into the atmosphere by water-splitting microorganisms. As you might recall from your biology courses, during photosynthesis, plants produce molecular oxygen, or O_2. As the O_2 increases in concentration, some of it is converted to ozone. This ozone rises in the atmosphere and provides a protective layer against the high-energy ultraviolet (UV) radiation from the sun.

Throughout the years, new, more complex life forms arose that had to adjust to the oxygen in the environment. Many organisms took advantage of O_2 and used it to increase their metabolic efficiency. However, there was a danger associated with O_2 in biological systems. A complex array of positive and negative effects of O_2 had to be addressed by these organisms. One of the consequences of O_2 utilization was the generation of a chemical species called free radicals.

The oxygen story

When a person suffers a heart attack, the heart muscle undergoes changes due to lack of blood and oxygen in the tissues. This damaged tissue is called an **infarction**. As the muscle heals, new blood vessels again are supplied and oxygen is available. Only within the last decade has it been learned that as a person recovers from a heart attack, the inflow of oxygen-laden blood is dangerous to the heart muscle. This process is known as **reperfusion oxidation**.

The cause of this danger was found to be free radicals produced by the oxygen. This phenomenon is called **reperfusion**, or **reoxygenation injury**. Now it's known that more chronic diseases are associated with oxygen toxicity and are related to free radical mechanisms. To understand free radical chemistry requires some knowledge of the oxygen reactions. So, let's start with the chemistry of oxygen as this journey begins.

The chemistry of oxygen

There is a mystery about chemistry that causes some people to fear it, almost as something occult, grossly complex and forbidding. Even the word turns many people off. In reality, it isn't so bad. When taken in small bites, it easily is assimilated—in fact, it can be palatable. Take oxygen, for example.

Oxygen is one of the most abundant materials both on earth and in the atmosphere. While it is essential for life, it also is quite toxic to many life forms. Even plants must be protected against the very oxygen they generate by photosynthesis. The usefulness of oxygen and its harmful effects are related to the chemistry of oxygen, which in turn relates to the molecular structure of oxygen. To understand this molecular structure is to appreciate the role that oxygen plays in free radical mechanisms. A free radical will be defined later, but first, let's take a look inside the oxygen molecule.

All molecules are composed of atoms, which are made up of smaller particles called protons, neutrons and electrons. The protons and neutrons are located in the nucleus of the molecule while the electrons are found in the orbital that whirls around the nucleus. These orbitals are not discrete, neat circles or layers, but rather they are specific energy levels. These energy levels are very real even though they are hard to visualize, or even localize, without using complex mathematics. As rapidly as it moves, a single electron is easily located. It forms a veritable cloud of energy paths around the nucleus. While this can seem chaotic at first glance, there are very strict laws that the electrons must obey. These laws were discovered during this century by some very brilliant scientists, who eventually created **quantum mechanics**, a physics discipline that is used to describe this subatomic activity. Fortunately, to be able to understand how quantum mechanics relates to free radical chemistry and oxygen toxicity, little more than the name of this discipline needs to be known.

Inside the oxygen molecule

One of the quantum mechanical laws requires that electrons be paired when they react with other electrons in another molecule—paired in the sense that within a given molecule, each electron is harmonious with another electron to keep the molecule stable. The oxygen molecule has two unpaired electrons, which makes it quite unique in nature and at the same time limits its ability to react with other molecules. This limitation of oxygen makes it relatively inert as far as its reactivity. This is a blessing, for if molecular oxygen were slightly more reactive, life as it is known would be impossible.

This same limitation does, however, have another side. It is the reason that oxygen enters into free radical reaction. Since most molecular reaction involves two electrons, oxygen cannot enter into these reactions except under very special circumstances. Oxygen is forced to react with one electron at a time because of this molecular limitation. ***This is a key concept in understanding free radical chemistry.***

A free radical is any atom or molecule that has one or more unpaired electrons and is capable of independent existence. Oxygen, then, is a free radical. In fact, oxygen is a **diradical**, which means it has two unpaired electrons.

Here, simplified, is the secret of the free radical—one or more unpaired electrons in a molecule or atom that can exist independently, and can react actively with other nearby molecules to alter or destroy them. An example will make this concept more graphic and easier to remember.

Water contains hydrogen and oxygen. It is a very simple molecule, and is written in chemical notation as either H_2O or HOH. The hydrogen atoms exactly balance the electronic charges in the oxygen atom to give us one molecule of water. If only one molecule of hydrogen would react with the oxygen molecule, a free radical would exist, the deadly hydroxyl radical ·OH. The little dot to the left of the “OH” formula means it is a free radical. This ·OH is called the hydroxyl radical and is a very nasty free radical because it reacts immediately with any molecule adjacent to it to alter or destroy it. It is a blessing that oxygen does not react with hydrogen in this manner to form hydroxyl radicals because life would be impossible if it did. It takes several steps and will be discussed later in the chapter.

Oxygen and respiration

When you breathe, you take in molecular oxygen, or O_2. It passes into the lungs and then into the blood stream to bind a pigment called **hemoglobin** in the red blood cells. This action makes the hemoglobin turn red. When this hemoglobin reaches the many cells of the body, it releases the molecular oxygen that diffuses through the capillaries into the cells. The cells release carbon dioxide into the capillaries and then bind to the hemoglobin, turning it blue. This is a very neat arrangement and quite effective for transporting oxygen safely.

Once the oxygen is in the cell, it can be utilized in many ways. The most important use, the one that uses about 98–99% of the oxygen you breathe, is the neutralization of electrons. These electrons are carried over from the metabolism of foods. When sugar, for example, is metabolized, energy is produced in each cell while electrons are released in the process. The molecular oxygen combines with these electrons in a highly specialized enzyme system called the electron transport system. It is this enzyme system, located in tiny organelles in the cell called mitochondria that adds electrons to the oxygen to produce water.

This process, called tetravalent reduction of oxygen to water, is a very special case for combining more than one electron with oxygen. Here oxygen will accept **four electrons** and produce two molecules of water, but only with the aid of these special enzymes. As these electrons are added to oxygen by the enzymes, a great deal of energy is produced with each step. This energy, in the form of adenosine triphosphate (ATP), is the energy source that runs the body. This is a very efficient system. Without it, multicellular organisms could not exist in great complexity.

However, about 1% of the oxygen you breathe is not used by this system, thus is available to wreak havoc with the rest of the body. This remaining oxygen can undergo several chemical changes that make it very unfriendly—in fact, quite dangerous. The changes in oxygen produce more reactive types of oxygen, which is called the reactive oxygen species.

The reactive oxygen species

The 1% of oxygen that does not enter the electron transport system is available to enter other reactions, mainly reactions that occur with oxygen accepting one electron. When a molecule or atom accepts an electron or hydrogen, this process is called **reduction**. On the other hand, when a molecule or atom loses an electron or hydrogen, this process is called **oxidation**.

These terms must be understood to appreciate the meaning of the one electron reduction of oxygen that results in forming **reactive oxygen species**, or ROS. The term reactive oxygen is used here because, as mentioned earlier in this chapter, normal oxygen is not very reactive. The **univalent reduction** of oxygen, or the addition of one electron at a time, produces these ROS. If a series of electrons is added to oxygen, four oxygen products with the formation of water as the fourth one is produced. Here is the scheme:

Oxygen + one electron = Superoxide (O_2-)

Superoxide + one more electron =
Hydrogen peroxide (H_2O_2)

Hydrogen peroxide + one more electron =
Hydroxyl radical (·OH)

Hydroxyl radical + one more electron + hydrogen =
Water (H_2O)

Three reactive oxygen species, or ROS, are seen, but only two are free radicals. These are the superoxide and the hydroxyl radical. Hydrogen peroxide is an ROS, but not a free radical. Do not be confused by this, since not all free radicals involve oxygen, and not all reactive oxygen is in the form of free radicals. The fourth type of ROS, known as **singlet oxygen**, will be discussed later in the chapter. For the moment, keep this concept in mind: ***Adding one electron at a time to oxygen produces three types of ROS, all of which are reactive and dangerous.*** Everything else will become clearer as you read on.

Let's return to the concepts of oxidation and reduction, since they are critical concepts in what shall follow. Oxygen, under normal conditions, can only react with one electron at a time, so there must be other chemicals that can react with it. There are, and one you are familiar with is **iron**.

Rusty iron is seen all the time, but only because oxygen can react with it. Rusty gold isn't seen because oxygen cannot react with it. Iron is called a **transition metal** because it can go from one molecular state to another molecular state by adding or losing an electron. These two states of iron are called Fe^{II} and Fe^{III}, or Fe^{2+} or Fe^{3+}. Years ago, these two forms were called ferrous iron (Fe^{2+}) or ferric iron (Fe^{3+}), but this terminology has lost favor.