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Retinal: The Biological Role and Significance

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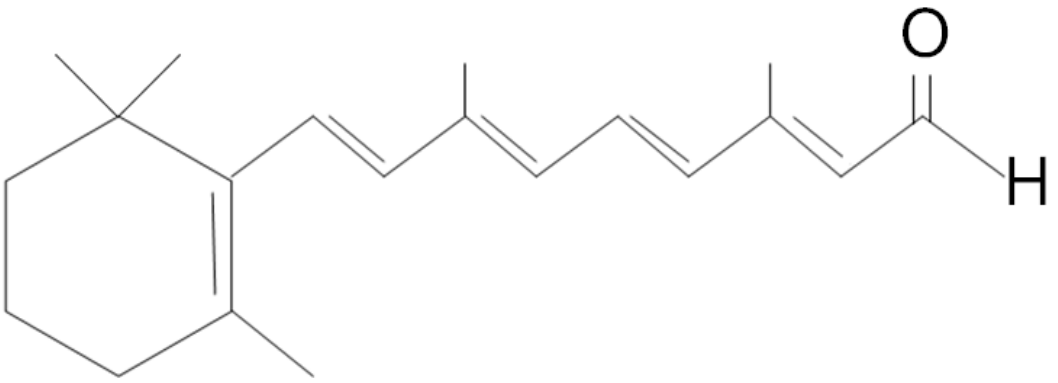
INTRODUCTION

Retinal, one of several vitamin A compounds serves a vital role in human vision (Tver and Russell, 458). Discovered in 1913, Vitamin A was the first vitamin to be discovered. The Vitamin A group includes the carotenoids, retinol and retinal. Each of these forms plays a significant role in animal vision, and vision is what led to vitamin A's discovery. During the early 1900s, many researchers were conducting studies on the eyes of animals. They found that if the animals were consuming diets deficient in what are recognized today as vitamin A-rich sources, the animals' eyes became inflamed and eventually infected. In 1932, scientists discovered beta carotene and found out that the body is able to convert it into vitamin A, and furthermore, it could be used to prevent eye disorders (Somer 18). However, this was merely the discovery of Vitamin A. It wasn't until 1967, when George Wald, a professor at Harvard University, and his colleagues began to seek an understanding of vision and vitamin A's role in the vision process that retinal was discovered. Wald's group studied the protein rhodopsin which is present in the rods. They broke the proteins down into molecular parts and discovered a protein called opsin and an organic chromophore known as retinal (Szaflarski). The structure of retinal is pictured below.

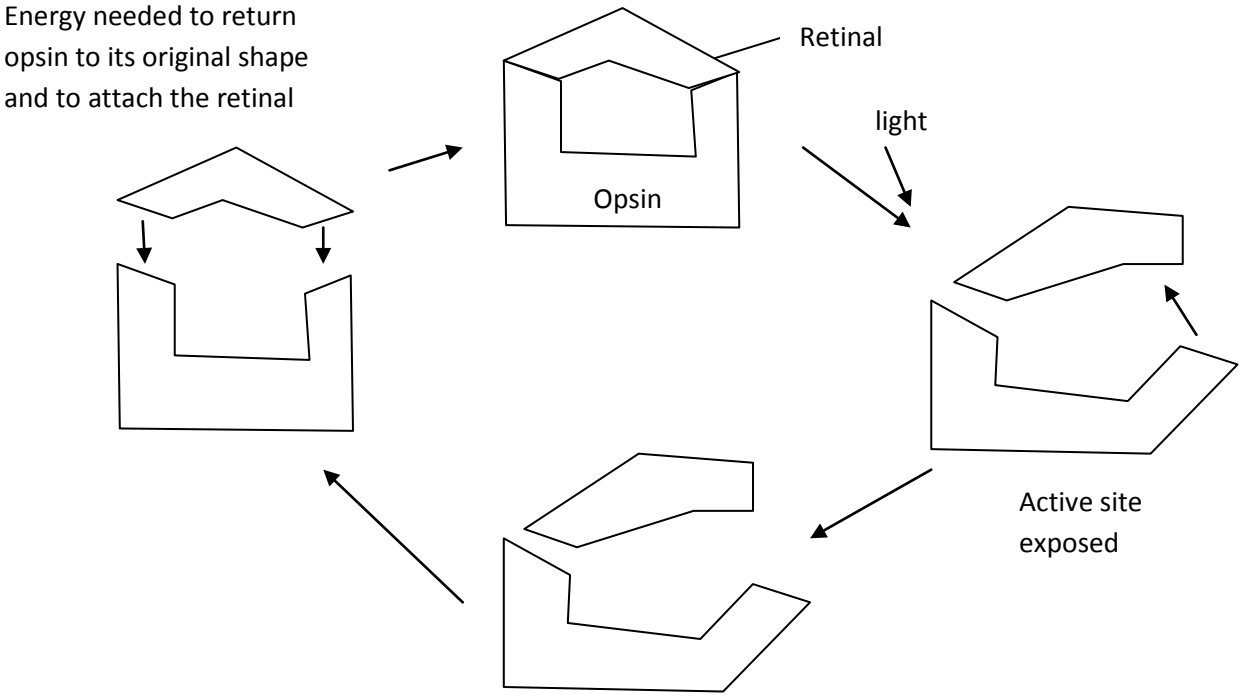
Retinal is an aldehyde, as the –al suffix suggests. By definition, an aldehyde must contain a carbon which is double-bonded to an oxygen atom, but that same carbon must also be bonded to at least one hydrogen atom. In order for this to occur, the afore-mentioned carbon must be on the end of a carbon chain. Otherwise, it would not be able to bond to a hydrogen atom. As one can see in the drawing on the following page, the carbon on the right fits the description. Thus it is an aldehyde. Additionally, there is a chain of carbons containing some double bonds. Those double bonds are indicative of the alkene functional group (Stoker 444).



Source: Stoker, H. S. (2010). *General, Organic, and Biological Chemistry* (5th Edition ed.). Belmont, CA: Brooks/Cole.

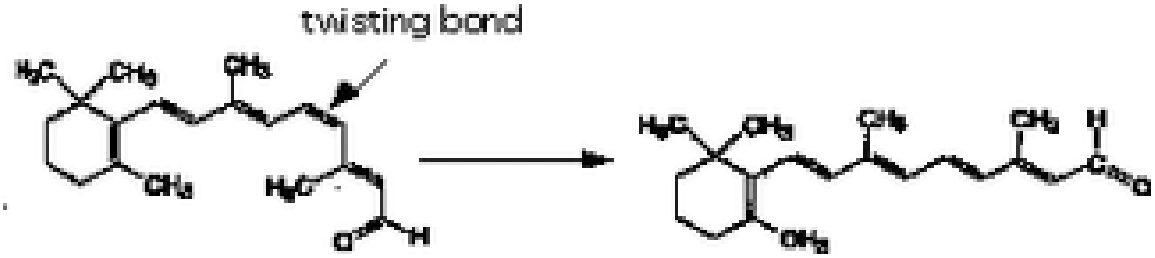
CHEMICAL REACTIONS OF RETINAL

Retinal plays an imperative role in human vision, and without its part in the rhodopsin cycle, sight would be impossible. Rhodopsin is the highly light-sensitive photopigment present in the rods of the eyes. When rhodopsin is exposed to any amount of light, it rapidly breaks down into a protein known as opsin and retinal. The light energy fuels a change in the potential of the rod cell membrane. This change causes both the retinal and the opsin to change their shapes, forcing the retinal to separate from the opsin. This separation exposes the active site of the opsin. The resulting signal travels to the brain and is interpreted as sight. Once the light source disappears or the person encounters darkness, the retinal reattaches to the opsin and is ready to be reactivated by light again. The rhodopsin cycle is pictured below (Thibodeau & Patton 392).



(Source: Adapted from Thibodeau & Patton 392)

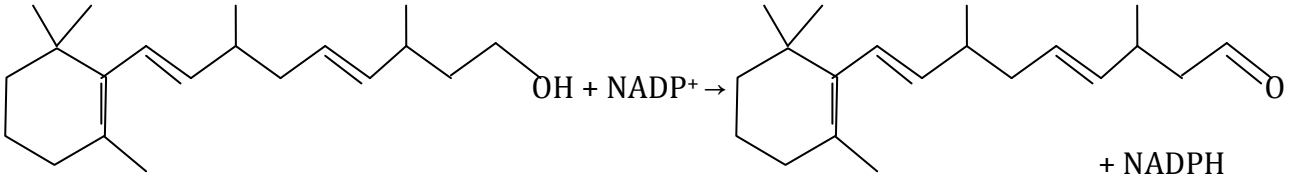
The retinal changes shape because it absorbs some of the light energy, forcing the molecule into a photo-excited state. The higher energy state causes one of the double bonds in the carbon chain to twist from 11-cis-retinal to 11-trans-retinal (Tver 460;



Szaflarski). The image below depicts the change in the chain which occurs when the molecule enters a higher energy state.

(Source: http://accessexcellence.org/AE/AEC/CC/vision_background.php)

Additionally, retinal can be converted to retinol through a reversible reaction with NADPH (Russell 460). Vitamin A is stored in the form of retinol, so when too much retinol is present, it is converted into retinal by the following reaction which is catalyzed by retinol dehydrogenases (RDH) and alcohol dehydrogenases:



In the above reaction, the RDH enables the H of the –OH (hydroxy) functional group at the end of the carbon chain to bond with the $NADP^+$ through an oxidation reaction (Wald 295).

Finally, retinal can undergo an oxidation reaction to form retinoic acid. This reaction requires retinal dehydrogenases and retinal oxidases to occur, and the reaction is as follows:

$$\text{Retinal} + O_2 + NAD^+ \rightarrow \text{retinoic acid} + H_2O_2$$

Retinoic acid does not serve a role in vision, but instead is found in bile or urine. Some research shows that retinoic acid may be needed to maintain the health of epithelial tissues (Tver 458).

BIOLOGICAL ROLES OF RETINAL

Human vision would not be possible without retinal. Retinal's role in the rhodopsin cycle is the key to sight (Tver 460). The rods of the eyes are found on some of the distal ends of the photoreceptor neurons on the retina. All rods contain a highly light-sensitive pigment known as rhodopsin, which is composed of two molecules: retinal and opsin. When rhodopsin is exposed to light, it breaks down into these two molecules, exposing an active site. The creation of this action potential triggers a neural impulse. The signal travels through a series of fibers to the virtual cortex in the occipital lobe of the brain for interpretation (Thibodeau & Patton 390-395). Without retinal, this process would not be possible and vision would not exist.

During the rhodopsin cycle, the retinal must dissociate from the opsin. Although most of the retinal is able to reattach to opsin molecules to repeat the rhodopsin cycle, some retinal is destroyed. In order to synthesize more retinal, people must consume vitamin A. The opsin in the rods is unable to function effectively without the retinal cofactor (Szaflarski). The bonding of retinal to opsin is what enables humans to see in the dark, otherwise known as night vision (Somer 19).

IMPORTANCE OF RETINAL

Though retinal is only involved in human vision, which is not necessary for life, its deficiency can result in grave consequences. The body synthesizes retinal from vitamin A, so retinal deficiency would most likely be a result of vitamin A deficiency. Chronic retinal deficiency can cause many problems with vision. Ulceration and/or distortion of the cornea as well as blindness can occur if the body is unable to produce retinal. This disease, known as xerophthalmia, starts out as a deformation of the conjunctiva, or the membranous covering of the eye. That membrane begins to thicken, wrinkle and dry out if it does not receive enough retinal. If the condition is not resolved at that point, the circumstances worsen as areas of the eye begin to harden. The eye then develops a milky appearance which causes an infection in the iris. The body develops scar tissue in response to this infection, and in turn causes blindness (Somer20-21).

Retinal is also involved specifically with night vision because of its role in the rhodopsin cycle. One of the first indicators of a retinal deficiency is the loss or deterioration of night vision. The rods can detect even the smallest amounts of light and produce vision in grayscale so that humans have at least some vision in near darkness (Thibodeau & Patton 392).

In order to develop a toxicity of retinal, a person would have to have over nutrition in vitamin A. The body synthesizes retinal among other molecules from vitamin A, so only its overconsumption could lead to retinal toxicity. However, the body has several natural processes to eliminate excess retinal, just as it has ways to eliminate other waste products. When too much retinal is present, it is converted to either retinoic acid, which remains in

bile or is excreted in urine, or it is converted to retinol, which is carried by the blood and eventually excreted in urine (Tver 460).

Despite the body's efforts to rid itself of waste and excess nutrients, toxicities can occur. Vitamin A toxicity is rare and is most often a result of supplement abuse. If vitamin A accumulates in the body, all of the forms of vitamin A accumulate, and that includes retinal. Toxic levels of these substances have been attributed to nausea, loss of appetite, hair loss, dry and cracked lips, liver enlargement, joint pain, abdominal discomfort and irritability.

Much is known about the biochemistry of sight. However; scientists and researchers are still hard at work to understand the various reactions in the eyes and how problems with specific reactions can cause blindness or eye disease. Though much is yet to be discovered, it is certain that vitamin A, and thus retinal, is vital to the health of human eyes and necessary for human sight (Szaflarski).

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This webpage is a part of the National Health Museum, a non-profit organization founded by former U.S. Surgeon General C. Everett Koop as a national center for health education. The author, Dr. Diane M. Szaflarski is an adjunct associate professor of chemistry at North Carolina Central University.

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