FEDERAL UNIVERSITY OF TECHNOLOGY MINNA

RETINOL : THE VITAMIN OF LIFE

Dean
Sch. of Sci. & Tech. Education
Federal University of Technology
Minna

By

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Inaugural Lecture Series No. 5

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Inaugural Lecture delivered at the
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Fellow Biochemists

Eminent Invited Guests

Ladies and Gentlemen

It is with humility and joy that I stand before you this day to deliver this inaugural lecture titled "Retinol, The Vitamin of Life".

I do understand that inaugural lectures afford one the opportunity to bring 'town and gown' together in a celebration of academic excellence, discussing one's contributions to knowledge in a language which is informative and can be understood by ordinary person who is neither a biochemist or a scientist. Therefore, I intend to make my presentation as simple as possible. Vice Chancellor Sir, I am of the opinion that precision is a true mark of scholarship, I hereby crave your indulgence to permit me to delve into the issue of the day.

RETINOL

HISTORICAL INTRODUCTION

In the 16th Century BC night blindness and eye disorders, which were well recognized in ancient Egypt, were treated by the topical application of juice squeezed from raw liver or by prescribing liver in the diet (Wolf, 1996). Also fishermen from Newfoundland have known for a long time that they navigate better at night if they eat cod liver. This

medical folklore was lost over the centuries and night blindness plagued armies throughout the world in the 19th Century BC. In 1913 the researchers found a substance that made one grow and see better. McCollumn and Davis,(1913) described the substance as fat 'Soluble A'. Later, they gave the substance the name vitamin A. Another growth promoting factor, vitamin A_2 (3-dehydro retinol) was also detected from fresh water fish liver oils. Since then researchers have continued to unravel the biochemical importance of this unique substance in metabolism.

The structure of Vitamin A was elucidated in 1930 by Karer *et al.* The biological conversion of ß-carotene into vitamin A was also demonstrated in the same year.

THE STRUCTURE OF RETINOL

The parent compound in the vitamin A group is called all-trans retinol. Retinol is the immediate precursor to two important active metabolites: retinal, which plays a critical role in vision, and retinoic acid, which serves as an intracellular messenger that affects transcription of a number of genes. ß-carotene is the major carotenoid that can be converted to vitamin A within the intestine and other tissues (Olson *et al.*, 2000). The structures of these compounds are presented in Figure 1.

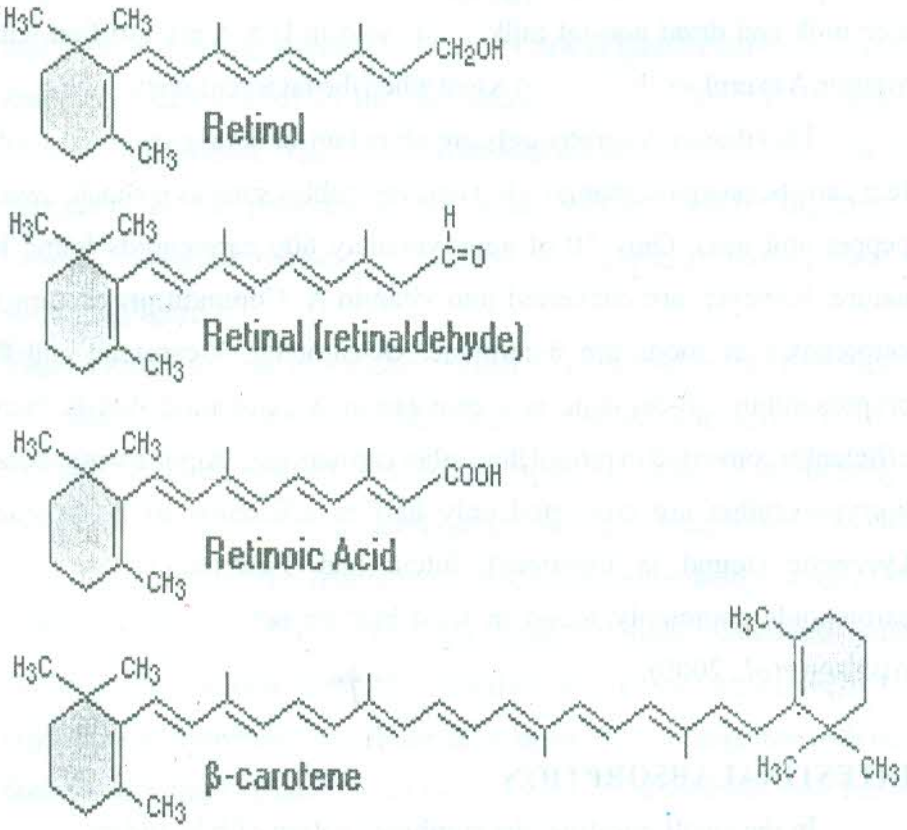

Figure 1. Structure of some vitamin A compounds.

SOURCES OF RETINOL

Retinol is often called preformed vitamin A while the carotenoids are the provitamin A.

Pre-formed vitamin A is found in animal foods such as whole eggs, cheese, whole milk and liver (Sebrell and Harris, 1967). Fortified

foods such as fortified breakfast cereals also provide vitamin A. Most fat-free milk and dried non-fat milk solids sold in U.S.A are fortified with vitamin A to replace the vitamin A lost when the fat is removed.

Provitamin A carotenoids are abundant in darkly coloured fruits (e.g carrots, pawpaw, mango, etc.) and vegetables such as spinach, sweet pepper and peas. Only 50 of approximately 600 carotenoids found in nature, however, are converted into vitamin A. Common provitamin A carotenoids in foods are ß-carotene, ∝-carotene, ϒ-carotene and ß-cryptoxanthin. ß-carotene is a provitamin A carotenoid that is more efficiently converted to retinol than other carotenoids. Alpha carotene and ß-cryptoxanthin are converted only half as efficiently as ß-carotene. Lycopene (found in tomatoes), lutein and 3-zeaxanthin are other carotenoids commonly found in food but are not sources of vitamin A(Olson *et al.*, 2000).

INTESTINAL ABSORPTION

In the small intestine, the combined action of bile and pancreatic esterases hydrolyses the esters of retinol. Retinol is then actively transported in micellar form across the membrane of epithelial cells of the intestinal villus (Ong, 1994). The absorption efficiency of dietary vitamin A in healthy person who ingest significant amounts of fat is >80%. The absorption efficiency, or bioavailability, of dietary carotenoids can vary from approximately 50% to <5% depending on the specific carotenoid, its isomeric form, the amount ingested, the presence of accompanying fat, cooking practice, the particle size of the ingested food and the integrity of the gut (de Pee and West, 1996). The absorption efficiency is best with

relatively small amounts of all-trans ß-carotene in oil, such as red palm oil, and poorest in whole vegetables, whether raw or rapidly stir-fried. As the amount of carotenoids in the diet increases, however, the absorption efficiency decreases. The intestinal absorption of carotenoids is critically dependent on the presence of bile acids (Olson, 1994). Ingested ß-carotenes may be oxidatively cleaved by ß-carotene dioxygenase as shown in Figure 2.

This cleavage utilizes molecular oxygen, is enhanced by the presence of bile salts, and generates two molecules of retinaldehyde (retinal). In the intestinal mucosa, retinal is reduced to retinol by a specific retinaldehyde reductase utilizing reduced nicotinamide adenine dinucleotide (NADH). A small fraction of the retinal is oxidized to retinoic acid. Most of the retinol is esterified with saturated fatty acids and incorporated into lymph chylomicrons, which enter the bloodstream. These are converted to chylomicrons remnants, which are taken up by the liver together with their content of retinol (Blaner and Olson, 1994). Carotenoids may escape some of these processes and pass directly into the chylomicrons.

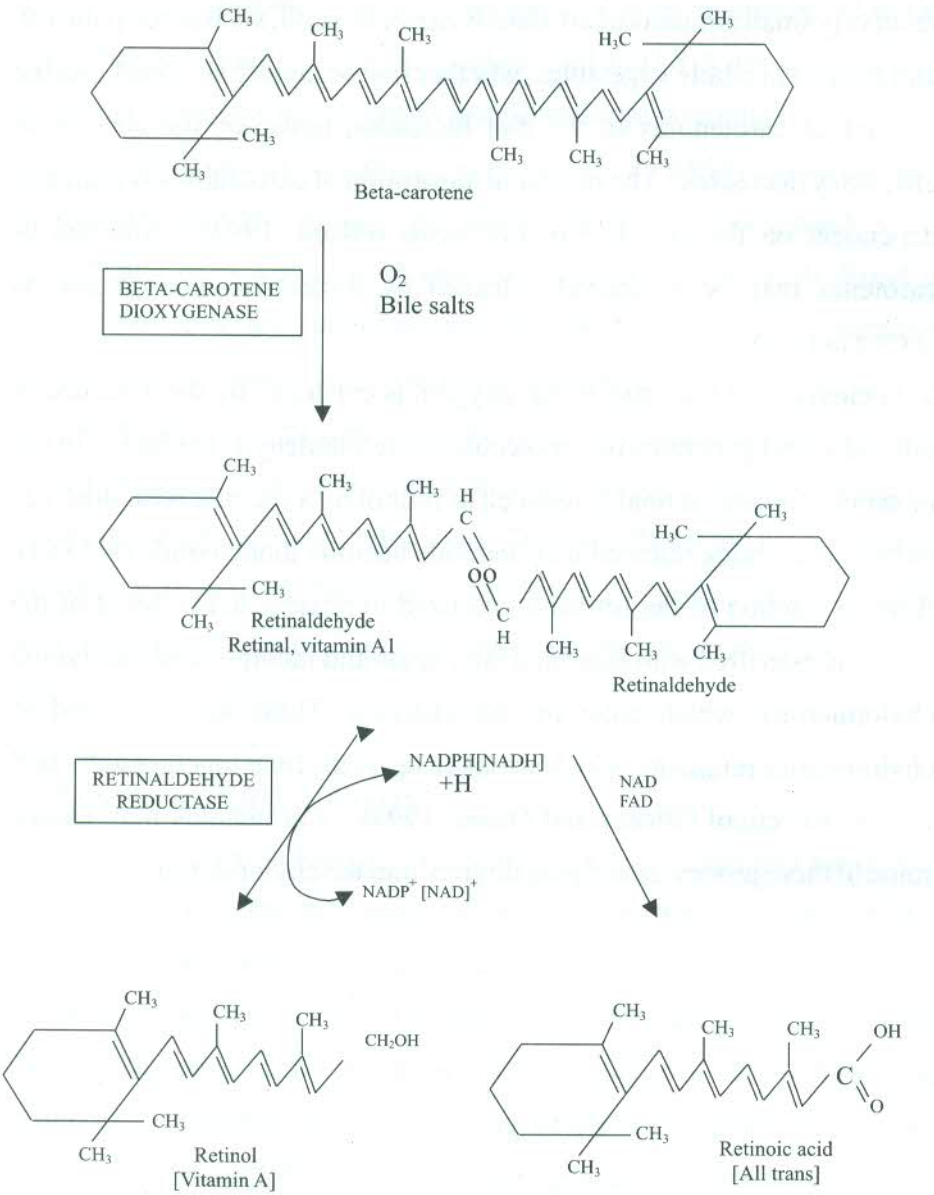

Fig 2. Conversion of ß-carotene to Retinol.

STORAGE OF RETINOL IN THE BODY

Hepatic vitamin A in a well-nourished individual normally represents over 90% of the total reserve of vitamin A in the body (Goodman, 1984). The parenchyma cells, the predominant cell type in the liver, contain small amounts of retinol and significant amounts of retinyl ester. These cells take up and process chylomicron remnants as well as synthesizing and releasing plasma retinol - binding protein (pRBP) (Blaner and Olson, 1994). Ingested vitamin A is therefore, transferred from parenchyma cells to stellate cells in the form of retinol, is then re-esterified, and stored there as a lipoglycoprotein complex. For its utilization, retinyl ester is hydrolysed to retinol, which is bound to apo-retinol binding protein (RBP) before it is released into the plasma.

Other important organs for vitamin A storage are the adrenals and the kidney. The adrenals contain stellate type cells similar to the liver. The kidney might not be a true storage organ since it is mainly involved in the metabolism of serum pRBP and the conservation of the retinol ligand. Another subsidiary storage site for retinol is the pigment epithelium of the retina in the eye. The retinol arrives from circulation as holo-retinol-binding protein (holo-RBP) and becomes esterified and stored in pigment epithelium in lipid droplets (Blaner and Olson, 1994).

TRANSPORT OF RETINOL IN THE PLASMA

Vitamin A must be transported to target tissues, since retinol is a fat-soluble molecule and is not readily soluble in aqueous environment. In addition, the polyunsaturated nature of the molecule makes it susceptible to oxidation. With its polar end and non-polar groups it is also easily

adsorbed onto membrane interfaces. Hence, a binding protein is required to solubilise retinol in the aqueous plasma and intracellular fluids, thus enabling the vitamin to reach tissue cells while at the same time affording some protection against oxidation.

Vitamin A is mobilized from liver stores and transported in plasma as retinol bound to retinol-binding protein (Chen *et al.,* 1986). In humans, retinol-binding protein is a single polypeptide chain with a molecular weight close to 21,000 daltons and with one binding site for one molecule of retinol (Kanai *et al.,* 1968). In plasma, most of the normally circulating pRBP is saturated with retinol and is referred to as holo-RBP. The protein moiety also has a binding site for attachment of the molecule to receptors on the target tissues such as pigment epithelia in the eye, epithelial cells of the skin and cells of the reproductive tissues. The protein, however, is small enough to be susceptible to glomerular filtration in the kidney and thus loss of retinol in circulation. Holo-RBP, however, is combined with prealbumin (transthyretin) also in 1:1 mole ratio raising the complex to approximately 75,000 daltons and thus preventing glomerular filtration in the kidney (Kanai et al., 1968).

The combination of retinol and pRBP protects and stabilizes the vitamin, makes it soluble and transportable in plasma and protects tissues from the toxicity of free retinol. The combination of prealbumin with holo-RBP further confers stability on the holo-RBP.

THE CONCENTRATION OF RETINOL-BINDING PROTEIN IN PLASMA.

The concentration of retinol in plasma is 30μg/100ml for normal