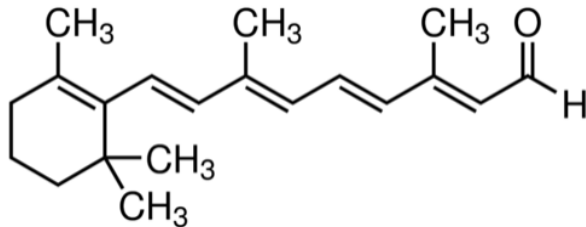


Vitamin A 25,000 IU

TECHNICAL SUMMARY

Vitamin A is a fat-soluble antioxidant vitamin that is required for normal vision as well as brain and bone development.* It is essential for healthy reproductive function, proper cell cycle regulation, and for the maintenance of skin and mucosal surface integrity.* Vitamin A is an essential nutrient for the support of healthy immune system performance, as well as for the rejuvenation of skin tissue.*

Structure Formula:



Chemical Name: all-*trans*-Retinol.

Allergen and Additive Disclosure: Not manufactured with yeast, wheat, gluten, soy, corn, milk, egg, shellfish or sesame ingredients. Produced in a GMP facility that processes other ingredients containing these allergens

Delivery Form: Softgels.

ROLE AS NUTRIENT/FUNCTION

Retinol and its derivatives are important for normal vision, gene expression, reproduction, growth, and immune function.* The retinal form of vitamin A is required by the eye for the transduction of light into neural signals necessary for vision, through its structural role in the visual pigment rhodopsin.* Vitamin A is also required to maintain the integrity of epithelial cells throughout the body via its metabolite, retinoic acid, which regulates expression of various genes that encode for structural proteins (e.g., skin keratins), enzymes (e.g., alcohol dehydrogenase), extracellular matrix proteins (e.g., laminin), and retinol binding proteins and receptors.* Retinoic acid is important in maintaining an adequate level of circulating natural killer cells and for the phagocytic activity of macrophages; it increases the production of IL-1 and other cytokines and stimulates production, growth, and differentiation of B lymphocytes.*

NATUROKINETICS®

Liberation: Dissolution of the softgel capsule is tested in water using a USP testing method with dissolution between zero and 60 minutes.

Absorption: Retinol's absorption takes place primarily in the small intestine by both saturatable and non-saturatable mechanisms. The saturatable transport is carried out via a specific retinol transport protein within the brush border. Independently of the dose, the efficiency of absorption of preformed vitamin A in the small intestine is generally high, in the range of 70 to 90%. In a pharmacokinetic trial conducted with volunteers from the U.S. and China, T_{max} was 12 h following a single administration of retinyl acetate (Figure 1).

Supplement Facts

Serving Size 1 Softgel

	Amount Per Serving	% Daily Value
Vitamin A (from Retinyl Palmitate and Fish Liver Oil)	7,500 mcg	833%

Other ingredients: Softgel Capsule [bovine gelatin (BSE-free), glycerin, water] and Organic Extra Virgin Olive Oil.

- **Healthy Immune Function***
- **Supports Eye and Skin Health***

SUGGESTED USAGE: Take 1 softgel every 3 days with a meal, or as directed by your healthcare practitioner.

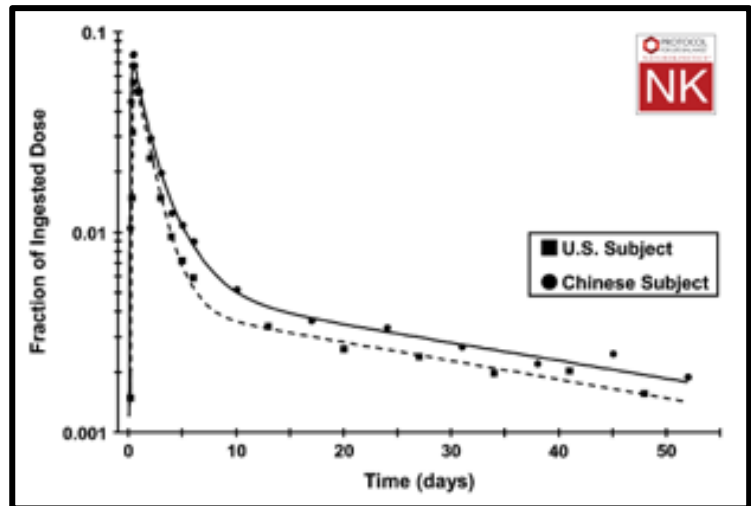


Figure 1 Mean observed (symbols) and model-predicted (lines) fraction of ingested dose in serum for a representative Chinese and U.S. subject vs. time (d) after a single administration of radiolabeled retinyl acetate (approx. 1,000 IU Vitamin A) in corn oil.

In a pharmacokinetic study with healthy adult volunteers, a single administration of 25,000 IU of vitamin A, T_{max} for free retinol was achieved at 36 hours post-administration (Figure 2). The decrease in free serum retinol concentration 12 hours post-administration is due to the ability of high doses of vitamin A to significantly increase the expression of retinol-binding proteins and retinol uptake by the liver.

Distribution: At least half the body's supply of retinol is stored in the liver in its esterified form through active uptake of retinyl esters by hepatocytes. To release retinol into circulation, retinol-binding protein (RBP) forms complexes with retinol, followed by complex formation with transthyretin present in the circulation to form a tri-molecular form. In this form, retinol is transported to various tissues, including the eye. Retinol that is not immediately released into the circulation by the liver is re-

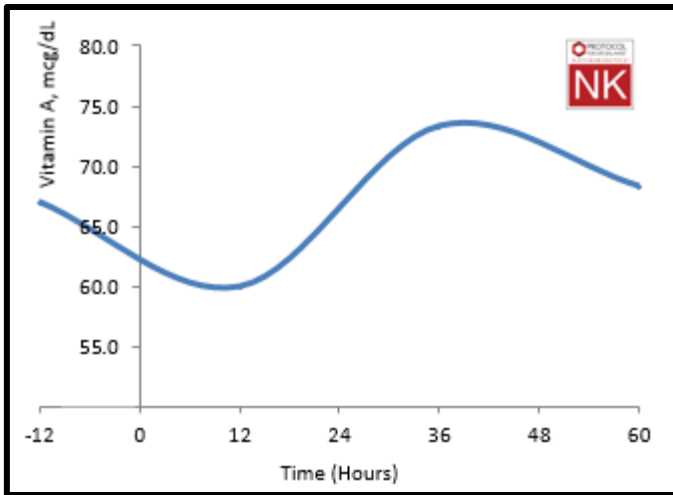


Figure 2. Average Vitamin A concentration (as free plasma retinol) in healthy adult volunteers 12 hours before and 12, 36, and 60 hours following a single administration of Vitamin A 25,000 IU softgel (P0340, Protocol for Life Balance®).

esterified and stored in the lipid-containing stellate cells of the liver until needed to maintain normal blood retinol concentrations.

Metabolism: The small intestine, liver, and peripheral tissues play crucial roles in vitamin A metabolism, with extensive inter-organ recycling of retinoids occurring among them. Newly absorbed vitamin A is rapidly and efficiently (85–90%) taken up into liver where it is either stored or freed for peripheral use depending on the body's needs. The liver is the main organ responsible for vitamin A's homeostasis in the body. Computer models have estimated that each molecule of retinol is recycled 9 to 11 times between the liver, plasma, kidneys, and other tissues before being irreversibly degraded. The catabolism of retinol, retinoic acid, and other carotenoids in the body is complex and involves multiple enzymatic processes both in the liver and peripheral tissues including microsomal cytochrome P450 enzymes.

Elimination: Biologically inactive metabolites of vitamin A, including glucuronic acid and taurine conjugates, are eliminated via urine and bile. The portion of excreted vitamin A metabolites in bile increases as the vitamin A content in the liver exceeds a critical concentration. This increased excretion has been suggested to serve as a protective mechanism for reducing the risk of excess storage of vitamin A.

CLINICAL VALIDATION

- **Immune System Support.*** In a randomized, double-blind study, women were treated with supplemental vitamin A for 4 months, and the effects on immune system functioning were observed by monitoring serum concentrations of IL-4 and IL-13. Results showed a significant decrease in serum concentrations for both IL-4 and IL-13, which suggests a role for vitamin A in promoting healthy immune system functioning (Figure 3).*

SAFETY INFORMATION

Tolerability: Tolerable Upper Intake Level (UL) for adults is set at 3,000 µg/day (10,000 IU) of preformed vitamin A. However, the UL is not meant

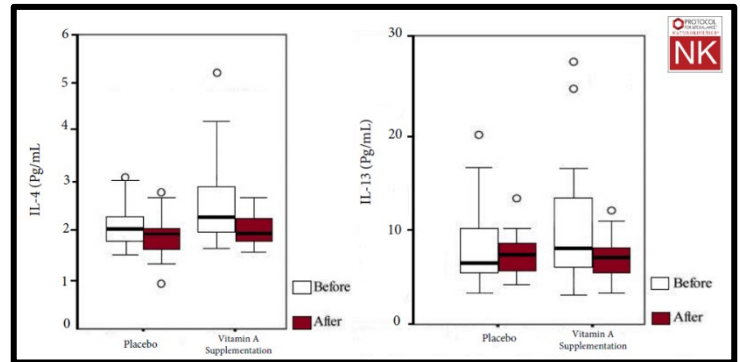


Figure 3: IL-4 and IL-13 serum concentrations determined by Wilcoxon signed-ranked test for placebo group and vitamin A treated group.

to apply to individuals who are receiving vitamin A under medical supervision.

Contraindications: None known.

INTERACTIONS

Drug Interactions: Vitamin A derivatives (i.e. acitretin, isotretinoin, tretinoin) could have additive effects when taken with vitamin A supplements. Taking high doses of vitamin A in combination with other potentially hepatotoxic drugs might increase the risk of liver adverse events. The latter may include acetaminophen, carbamazepine, methotrexate, methyldopa, and many others. Co-administration of high doses of vitamin A and tetracyclines may increase the risk of benign intracranial hypertension. High doses of vitamin A could increase the risk of bleeding with warfarin, possibly due to vitamin K antagonism. Orlistat can decrease absorption of fat soluble vitamins including vitamin A, leading to low plasma levels in some patients. All patients taking orlistat are recommended to take a multivitamin supplement containing all the fat soluble vitamins, separating the dosing time by at least 2 hours from Orlistat.

Supplement Interactions: Dietary fat increases vitamin A absorption. Taking high doses of vitamin A in combination with other potentially hepatotoxic dietary supplements might increase the risk of liver adverse events.

Interaction with Lab Tests: Vitamin A supplementation may cause a false increase in bilirubin test results.

STORAGE

Store in a cool, dry place in original sealed container.