The Role of Systemic Vitamin Supplementation as a Therapeutic Adjuvant in the Treatment of Some Dermatological Diseases

E S S A Y

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بسم الله الرحمن الرحيم

قَالُوا سُبْحَانَكَ لاَ عِلْمَ لَنَا
إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ
الْعَلِيمُ الْحَكِيمُ

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ABSTRACT

Vitamins are organic compounds that are biologically active and indispensable for normal physiologic functions. Vitamins do not have a direct role as an energy source, but they act as coenzymes of cellular metabolic processes essential for the adequate functioning and growth of tissues.

As essential nutrients, they must be supplied exogenously. In developed countries, vitamin deficiencies are usually the result of metabolic or organic disorders, whereas hypervitaminosis is usually self induced. In developing countries, vitamin deficiencies are primarily linked to malnutrition. Either an excess or deficiency of particular vitamins may cause dermatologic disease.

The vitamins are mainly classified into: (1) The fat soluble vitamins designated as A,D,E and K, and (2) water soluble vitamins known as B complex and C.

Fat soluble vitamins include (A, D, E and K) which can be used as an adjuvant therapy in the treatment of some dermatological diseases as acne, psoriasis, disorders of keratinization and photocarcinogenic diseases.

Water soluble vitamins include (C and B complex) which its main actions as antioxidant agents can be used as an adjuvant therapy in the treatment of some dermatological diseases as aging of the skin and skin cancer.

Key words:

Fat soluble - Water soluble - Vitamins – Skin - Adjuvant

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List of Abbreviation

$1,25(OH)_2D_3$	Calcitriol
25-hydroxy cholecalciferol	Calcidiol
AA	Ascorbic acid
ACP	Acyl carrier protein
AI	Adequate intake
AMD	Age-related macular degeneration
APCs	Antigen presenting cells
AR	Amphiregulin
ATF	Anti-thiamine factor
AThDP	Adenosine thiamine diphosphate
AThTP	Adenosine thiamine triphosphate
ATP	Adenosine triphosphate
BCC	Basal cell carcinoma
BMD	Bone mass density
CAT	Catalase
CF	Cystic fibrosis
CLA	Cutaneous lymphocyte-associated antigen expression
CN	Cyanide
CoA	Coenzyme A
CRBP	Cellular retinoic acid binding protein
CRH	Corticotrophin-releasing hormone
CRP	C-reactive protein.
DCs	Dendritic cells
DFE	Dietary folate equivalent
DHT	Dihydrotachysterol
DRI	Dietary reference intakes
EGF	Epidermal growth factor
EGR	Erythrocyte glutathione reductase
FAD	Flavin adenine dinucleotide
FDA	Food and drug administration
FMN	Flavin mononucleotide
FNB	Food and nutrition board
G6PD	Glucose-6-phosphate deficiency
GABA	Gamma amino butyric acid
GERD	Gastrointestinal reflux disease
GPx	Glutathione peroxidase
GR	Glutathinone reductase
GSH	Glutathione
GTP	Guanosine-5-triphosphate

HCS	Holocarboxylase synthetase
Hcy	Hemocysteine
HER	Human epidermal growth factor receptor
HP	Hydroxyproline
HPLC	High performance liquid chromatography
HRE	Hormone responsive elements
IBD	Inflammatory bowel disease
IDDM	Insulin-dependant diabetes mellitus
IF	Intrinsic factor
IFN	Interferon
IFN-β	Interferon beta
IFN-γ	Interferon gamma
IL	Interleukin
INR	International normalized ratio
IRBP	Interphotoreceptor retinal-binding protein
KGF	Keratinocyte growth factor
KLC	Keratosis lichenoides chronica
LDL	Low-density lipoprotein
LO	Lysyl oxidase
LXR	Liver X receptor
MM	Malignant melanoma
MMA	Methyl malonic acid
MSH	Melanocyte-stimulating hormone
MTR	5 methyl tetrahydrofolate - homocysteine methyl transferase
MUT	Methylmalonyl coenzyme A mutase
NAD	Nicotinamide adenine dinucleotide
NADP	Nicotinamide adenine dinucleotide phosphate
NE	Niacin equivalent
NIA	Neuroleptic-induced akinesia
NSAIDs	Nonsteroidal anti-inflammatory drugs
NTD	Neural tube defects
OFR	Oxygen free radicals
OGDH	Oxoglutarate dehydrogenase
OI	Osteogenesis imperfecta
PABA	Para amino benzoic acid
PARPs	Poly-ADP-ribose polymerase
PDGF	Platelet derived growth factor
PDH	Pyruvate dehydrogenase
PKC	Protein kinase C
PKU	Phenylketonuria
PL	Pyridoxal
PLP	Pyridoxal 5-phosphate

PM	Pyridoxamine
PMS	Premenstrual syndrome
PN	Pyridoxine
POMC	Proopiomelanocortin
PT	Prothrombin time
PTH	Parathyroid hormone
PTHrP	Parathyroid hormone-related protein
RA	Retinoic acid
RAE	Retinol activity equivalents
RAL	Retinaldehyde
RANTES	Regulated on activation, normal T expressed and secreted small inducible cytokine
RAREs	Retinoic acid response elements
RARs	Retinoic acid receptors
RBP	Retinol-binding protein
RDA	Recommended dietary allowance
ROS	Reactive oxygen species
RXRs	Retinoic X receptors
SAD	Seasonal affective disorder
SAM	S-adenosyl methionine
SC	Stratum corneum
SC	Skin cancer
SCC	Squamous cell carcinoma
SLE	Systemic lupus erythematosus
SOD	Superoxide dismutase
TBP	Thiamine-binding protein
TDP	Thiamine diphosphate
TEWL	Transepidermal water loss
TG	Triglyceride
TGFβ	Transforming growth factor beta
THF	Tetrahydrofolate
TMP	Thiamine monophosphate
TNF	Tumor necrosis factor
TPN	Total parenteral nutrition
TPP	Thiamine pyrophosphate
TR	Thyroid receptor
TTP	Thiamine triphosphate
UL	Tolerable upper level
VDBP	Vitamin D binding protein
VDR	Vitamin D receptor
Vitamin D2	Ergocalciferol
Vitamin D3	Cholecalciferol
WKS	Wernicke-korsakoff syndrome

Introduction

There are four fat-soluble vitamins are: Vitamin A (Beta Carotene or Retinol), vitamin D, vitamin E and vitamin K. These vitamins are soluble in fat and are stored in the body. For this reason, an excessive amount of these vitamins can be toxic ***(Ferri, 2001)***.

There are two forms of vitamin A, Retinol and Beta-Carotene. Retinol is found only in foods of animal origin and Beta-Carotene is found in foods of both plant and animal origins. Vitamin A is necessary for good night vision, healthy skin and linings of the mouth, nose and throat, digestive and urinary tracts. It is also important for helping the body resist infection, promoting growth and maintaining teeth, hair, bones and glands. Deficiency symptoms include night and glare blindness, permanent blindness and rough, dry skin. Good sources of vitamin A are liver, dark green leafy and yellow vegetables (broccoli, carrots, winter squash), apricots, cantaloupe, milk, cheese, butter, fortified margarine and eggs. Taking large doses of vitamin A supplements can be dangerous. Symptoms of toxicity include headaches, vomiting, peeling of skin, oedema, skin textural changes, loss of body hair and enlargement of liver and spleen ***(Ferri, 2001)***.

Vitamin D is important for the body's absorption of calcium and phosphorus which are the two minerals needed to keep bones and teeth healthy. Deficiency symptoms include soft bones, bowed legs, poor teeth and rickets. The main source of vitamin D is found in fortified milk; however, fish liver oils, egg yolk, salmon, tuna and sardines also contain this vitamin. Vitamin D is also produced by the body with sunlight and is often referred to as the "Sunshine Vitamin". Vitamin D requirements can

be met by sunlight alone or a combination of food and sun. However, after a suntan is established, vitamin D production through the sun is stopped. Excess amounts of this vitamin can cause loss of appetite, vomiting, diarrhea, weight loss and kidney damage ***(Ferri, 2001)***.

Vitamin E protects tissue fats and vitamin A and vitamin C from destructive oxidation. It also helps maintain the body's cell membranes. Deficiency symptoms of vitamin E, although extremely rare, are oedema, irritability and anemia. Deficiency mostly occurs in premature infants. Vitamin E is found in polyunsaturated fats such as oils and margerines, whole-grain cereals, wheat germ, leafy green vegetables, nuts, seeds and beans. It is added to some foods as a preservative to prolong self life. Vitamin E is relatively nontoxic; however, too much of it can cause fatigue, headaches, dizziness and blurred vision accompanied by nausea ***(Ferri, 2001)***.

Vitamin K plays an important role in blood coagulation. Deficiency symptoms are slow blood clotting and hemorrhagic disease in a newborn. Vitamin K is found in dark leafy vegetables, soybean oil, other vegetable oils, wheat bran, tomatoes and cauliflower. It is relatively nontoxic but synthetic forms at high doses may cause jaundice. More than 500 micrograms is not recommended ***(Ferri, 2001)***.

There are nine water-soluble vitamins, eight of which are B-vitamins. They are: Vitamin C (Ascorbic Acid), vitamin B1 (Thiamine), vitamin B2 (Ribolflavin), Vitamin B3 (Niacin), vitamin B5 (Pantothenic Acid), vitamin B6 (Pyridoxine), vitamin B7 (Biotin), vitamin B9 (Folacin) and vitamin B12 (Cyanocobalamin). Water-soluble vitamins are vitamins that are not stored in the body. They are easily destroyed during storage and preparation and therefore need to be replenished frequently. Cooking and soaking foods in water leaches out B-vitamins, vitamin C

and minerals. Exposure to light destroys folacin, Riboflavin, Pyridoxine, vitamin B12 and vitamin C. Minimizing heat and cooking time greatly helps to preserve these vitamins. Water-soluble vitamins are found in a variety of food such as fruits, vegetables, whole grains and meats ***(Ferri, 2001)***.

Aim of the Work

As demonstrated, we notice that vitamins have multiple effects on different body systems including the skin. In the past few years, it has been noticed that many dermatological prescriptions contain more than one vitamin for diseases other than vitamin deficiency disorders. The aim of our work is to highlight the different actions of the most commonly prescribed vitamins in order to scientifically justify the increase in the use of these oral vitamins in various dermatological diseases and may suggest new indications.

Vitamin (A)

Synonyms:

Synonyms: 3,7-dimethyl-9-(2,6,6, trimethyl-1-cyclohexan-1-yl)-2,4,6,8-natetraen-1-0l, 3-dehydroretinol, antixerophthalamic vitamin, axerophtholum, beta-carotene oleo vitamin A, retinaldehyde (RAL), retinyl acetate, vitaminum A**,** retinyl palmitate, vitamin A, vitamin A1, vitamin A USP ***(Van den Berg et al., 2002)***.

Sources:

There are two types of vitamin A sources: (1) Natural, (2) Supplemental ***(Van den Berg et al., 2002)***. In the natural sources, there are two basic forms of vitamin A: Retinoids and Carotenoids. The retinoids, which are the active types, are contained in animal sources including meat, milk and eggs. Liver is particularly rich in retinoids, since it is one of the storage sites for excess. The carotenoids, which are the precursor forms of the vitamin are found in leafy green produce as spinach and turnip green, orange, sweet potatoes and carrots. Very fresh foods have the highest levels, followed by frozen foods. Typically, canned produce has little vitamin A. Preparing vegetables by steaming, baking or grilling helps them to release the carotenes they contain. Alpha and beta carotene, as well as some of the other lesser-known carotenoids, can be converted to vitamin A in the small intestine. This is done by the body on an "as-needed basis", so there is no risk of overdose as there is with the active form ***(Van den Berg et al., 2002)***.

In the supplemental sources, supplements may contain either the active or precursor forms of vitamin A. The active form may be more

desirable for those who may have some difficulty in converting the carotenoids into the active vitamin. This is more often true in those over age 55 or who have a condition that impairs the absorption of fat. There is a water-soluble form of the vitamin, retinyl palmitate, which may be better utilized in the latter case. Carotenes are also available either as oil-based or natural water-based formulas which have to be stored away from light and heat, to avoid their destruction ***(Van den Berg et al., 2002)***.

In developing countries, carotenoids from vegetables and fruits are the predominant source of vitamin A, e.g., 6 μg of carotene are equivalent to l μg of retinol. A high intake of carotenoid-rich foods such as carrots may induce carotenemia with orange-yellow skin pigmentation (carotenoderma). Other fruits or vegetables, such as tomatoes and papaya, may induce a similar condition, so called lycopenemia (due to an excess of lycopene). The term carotenemia is also used to designate the inability to convert ingested B-carotene into vitamin A (which can occur in patients with diabetes mellitus or hypothyroidism). It has also been reported in patients with anorexia nervosa ***(Monk, 1982).***

Carotenoderma is clinically apparent when carotene levels are three to four times the normal. Children develop carotenoderma more readily than do adults, often due to the consumption of prepared baby food containing orange vegetables. Carotenes are deposited in areas with abundant sebaceous glands (nasolabial folds, forehead) and in areas where the horny layer of the skin is thickest (palms and soles); as a result the yellow-orange to golden colour is most obvious in latter sites. Total serum carotenoids (normal range: 0.4-1.5 mg/L) will differentiate carotenemia from other conditions, such as jaundice, in which mucous membranes are stained yellow (most apparent in the sclera) and the tint of the skin is bronze, saffron or green. Carotenemia of dietary origin is