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Reviewing Therapeutic and Immuno-Pathological Applications of Vitamins and Carotenoids

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ABSTRACT

The present review is based mainly on papers published between 2000 and 2020 and gives information about the properties of the Vitamins and Carotenoids in chemical and biological systems and its possible role in preventing several diseases. The main aim of this report is to highlight its role as an immunopathological applications, also reported are bioactive properties that may influence the development of foam cells and protection against endothelial cell damage.

Therapeutic applications of Vitamin D[1–10]

Keywords : Bioactive, Endothelial Cell, Vitamin D

I. INTRODUCTION

Vitamin D is a fat-soluble vitamin that is naturally present in very few foods, added to others, and available as a dietary supplement. It is also produced endogenously when ultraviolet rays from sunlight strike the skin and trigger vitamin D synthesis. Vitamin D obtained from sun exposure, food, and supplements is biologically inert and must undergo two hydroxylations in the body for activation. The first occurs in the liver and converts vitamin D to 25-hydroxyvitamin D [25(OH)D], also known as calcidiol. The second occurs primarily in the kidney and forms the physiologically active 1,25-dihydroxyvitamin D [1,25$(OH)_2$D], also known as calcitriol.

Without sufficient vitamin D, bones can become thin, brittle, or misshapen. Vitamin D sufficiency prevents rickets in children and osteomalacia in adults. Together with calcium, vitamin D also helps protect older adults from osteoporosis. Vitamin D has other roles in the body, including modulation of cell growth, neuromuscular and immune function, and reduction of inflammation.

Inherited variation in Vitamin D genes is associated with predisposition to autoimmune disease type 1 diabetes

Jason d. Cooper, deborah j. Smyth, neil m. Walker, helen stevens, oliver s. Burren, chris wallace, christopher greissl, elizabeth ramos-lopez, elina

hyppönen, david b. Dunger, timothy d. Spector, willem

h. Ouwehand, thomas j. Wang, klaus badenhoop, and john a. Todd

Objective—Vitamin D deficiency (25-hydroxyVitamin D [25(oh)d] ,50 nmol/l) is
commonly reported in both children and adults worldwide, and growing evidence indicates that Vitamin D deficiency is associated with many extraskeletal chronic disorders, including the autoimmune diseases type 1 diabetes and multiple sclerosis.

Research design and methods—we measured 25(oh)d concentrations in 720 case and 2,610 control plasma samples and genotyped single nucleotide polymorphisms from seven Vitamin D metabolism genes in 8,517 case, 10,438 control, and 1,933 family samples. We tested genetic variants influencing 25(oh)d metabolism for an association with both circulating 25(oh)d concentrations and disease status.

Results—type 1 diabetic patients have lower circulating levels of 25(oh)d than similarly aged subjects from the british population. Only 4.3 and 18.6% of type 1 diabetic patients reached optimal levels ($75 nmol/l) of 25(oh)d for bone health in the winter and summer, respectively. We replicated the associations of four Vitamin D metabolism genes (gc, dhcr7, cyp2r1, and cyp24a1) with 25(oh)d in control subjects. In addition to the previously reported association between type 1 diabetes and cyp27b1 (p = 1.4 3 1024), we obtained consistent evidence of type 1 diabetes being associated with dhcr7 (p = 1.2 3 1023) and cyp2r1 (p = 3.0 3 1023).

Meta-analysis of the association between Vitamin D and autoimmune thyroid disease

Jiying wang, shishi lv, guo chen, chenlin gao, jianhua he, haihua zhong and yong xu

We identified all studies that assessed the association between Vitamin D and aitd from pubmed, embase, central, and china national knowledge infrastructure (cnki) databases. We included studies that compared Vitamin D levels between aitd cases and controls as well as those that measured the odds of Vitamin D deficiency by aitd status. We combined the standardized mean differences (smd) or the odds ratios (or) in a random effects model. Twenty case-control studies provided data for a quantitative meta-analysis. Compared to controls, aitd patients had lower levels of 25(oh)d (smd: –0.99, 95% ci: –1.31, –0.66) and were more likely to be deficient in 25(oh)d (or 2.99, 95% ci: 1.88, 4.74). Furthermore, subgroup analyses result showed that gd and ht patients also had lower 25(oh)d levels and were more likely to have a 25(oh)d deficiency, suggesting that low levels of serum 25(oh)d was related to aitd.
Methods: bibliographic search, eligibility criteria and excluded studies, data extraction, statistical method.

Micronutrients in autoimmune diseases- possible therapeutic benefits of zinc and Vitamin D
Inga wessels, lothar rink

This article provides an overview of general concepts of triggers and underlying mechanisms leading to self-destruction. Lately, several original concepts of disease etiology were revised and there is a variety of hypotheses on triggers, underlying mechanisms and preventive actions.

This article concentrates on the importance of nutrition, especially zinc and Vitamin D, for balancing the immune function. Homespun nutritional remedies

seem to re-enter today's therapeutic strategies. Current treatment approaches are largely symptomatic or suppress the immune system. However, recent studies reveal significant benefits of nutrition-related therapeutic approaches including prevention and treatment of established disease, which offers a cost-efficient and trigger-unspecific alternative addressing balancing rather than suppression of the immune system. Zinc and Vitamin D are currently the best studied and most promising candidates for therapeutic intervention.

Mounting evidence for Vitamin D as an environmental factor affecting auto immune disease prevalence

Margherita t. Cantorna and brett d. Mahon

This review discusses the accumulating evidence pointing to a link between Vitamin D and autoimmunity. Increased Vitamin D intakes might decrease the incidence and severity of autoimmune diseases and the rate of bone fracture. The optimal level of Vitamin D intake required to support optimal immune function is not known but is likely to be at least that required for healthy bones. Experimentally, Vitamin D deficiency results in the increased incidence of autoimmune disease. Mechanistically, the data point to a role for Vitamin D in the development of self-tolerance. The Vitamin D hormone (1,25-dihydroxy Vitamin D3) regulates t helper cell (th1) and dendritic cell function while inducing regulatory t-cell function. The net result is a decrease in the th1-driven autoimmune response and decreased severity of symptoms.

Pathophysiological role and therapeutic implications of Vitamin D in autoimmunity focus on chronic aid

Mattia bellan, laura andreoli, chiara mele, pier paolo sainaghi, cristina rigamonti, silvia piantoni, carla de benedittis, gianluca aimaretti, mario pirisi and paolo marzullo

In the present paper, we reviewed the current evidence regarding Vitamin D role in the pathogenesis and management of different autoimmune diseases. Consequently, it is not established if Vitamin D status is a factor involved in the pathogenesis of immune-mediated diseases and if cholecalciferol supplementation acts as an adjuvant for autoimmune diseases. The development of autoimmunity is a heterogeneous process, which may involve di_erent organs and systems with a wide range of clinical implications.

Vitamin D actions on cd4+ t cells in autoimmune disease

Colleen elizabeth hayes, shane l. Hubler, jerott r. Moore, lauren e. Barta, corinne e. Praska and faye e. Nashold

This review summarizes and integrates research on Vitamin D and cd4c t-lymphocyte biology to develop new mechanistic insights into the molecular etiology of autoimmune disease. A deep understanding of molecular mechanisms relevant to gene–environment interactions is needed to deliver etiology-based autoimmune disease prevention and treatment strategies. Evidence linking sunlight, Vitamin D, and the risk of multiple sclerosis and type 1 diabetes is summarized to develop the thesis that Vitamin D is the environmental factor that most strongly influences autoimmune disease development. Evidence for cd4c t-cell involvement in autoimmune disease pathogenesis and for paracrine calcitriol signaling to cd4c t lymphocytes is summarized to support the thesis that calcitriol is sunlight's main protective signal transducer in autoimmune disease risk. Animal modeling and human mechanistic data are summarized to support the view that Vitamin D probably influences thymic negative selection, effector th1 and th17 pathogenesis and responsiveness to extrinsic cell death signals, foxp3ccd4c t-regulatory cell and cd4c t-regulatory cell type 1 (tr1) cell

functions, and a th1–tr1 switch. The proposed th1–tr1 switch appears to bridge two stable, self-reinforcing immune states, pro- and anti-inflammatory, each with a characteristic gene regulatory network. The bi-stable switch would enable t cells to integrate signals from pathogens, hormones, cell–cell interactions, and soluble mediators and respond in a biologically appropriate manner. Finally, unanswered questions and potentially informative future research directions are highlighted to speed delivery of etiology-based strategies to reduce autoimmune disease.

Vitamin D in autoimmune, infectious and allergic diseases- a vital player

Tom l. Van belle, conny gysemans and chantal mathieu

In this review, we summarize the genetic and epidemiologic data potentially linking Vitamin D to autoimmune, infectious and allergic diseases. We also discuss how Vitamin D influences the immune responses in each of those conditions based on the data generated using patient samples or preclinical models of each of these diseases.

Vitamin D in systemic and organ-specific autoimmune disease

Nancy agmon-levin, emanuel theodor, ramit maoz segal and yehuda shoenfeld

Vitamin D has been defined as natural immune modulators, and upon activation of its receptors (vdrs), it regulates calcium metabolism, cellular growth, proliferation and apoptosis, and other immunological functions. In addition, vdrs' polymorphisms observed in some of these autoimmune diseases may further support a plausible pathogenic link. Notably, for some autoimmune disease, no correlation with Vitamin D levels could be confirmed.

In the current review we present the body of evidence regarding the plausible roles of Vitamin D and vdr's polymorphism in the pathogenesis of autoimmunity. We summarize the data regarding systemic (i.e., systemic lupus erythematosus, rheumatoid arthritis, etc.) And organ-specific (i.e., multiple sclerosis, diabetes mellitus, primary biliary cirrhosis, etc.) Autoimmune diseases, in which low level of Vitamin D was found comparing to healthy subjects. In addition, we discuss the correlations between Vitamin D levels and clinical manifestations and/or activity of diseases. In this context, we address the rational for Vitamin D supplementation in patients suffering from autoimmune diseases. Further studies addressing the mechanisms by which Vitamin D affects autoimmunity and the proper supplementation required are needed.

Vitamin D, autoimmune disease and rheumatoid arthritis

Stephanie r. Harrison, danyang li, louisa e. Jeffery, karim raza, martin hewison

The aim of this review is to explore the immune activities of Vitamin D that impact autoimmune disease, with specific reference to ra. As well as outlining the mechanisms linking Vitamin D with autoimmune disease, the review will also describe the different studies that have linked Vitamin D status to ra, and the current supplementation studies that have explored the potential benefits of Vitamin D for prevention or treatment of ra. The overall aim of the review is to provide a fresh perspective on the potential role of Vitamin D in ra pathogenesis and treatment.

Vitamin D, invariant natural killer t-cells and experimental autoimmune disease

Margherita t. Cantorna, jun zhao and linlin yang

Vitamin D is an important regulator of the immune system in general and multiple sclerosis. Experimentally (i), invariant natural killer t (inkt) cells

have been shown to be important suppressors of autoimmune diseases such as experimental autoimmune encephalomyelitis (eae; an animal model of multiple sclerosis). Conversely, in experimental allergic asthma inkt cells are required for disease induction and are therefore pathogenic. The active form of Vitamin D (calcitriol) suppresses eae. The development of eae symptoms is accelerated in Vitamin D deficiency. Interestingly experimental asthma is less severe in Vitamin D deficiency although there is no effect of calcitriol on disease severity. The data suggest that an important target of Vitamin D in eae and asthma are the inkt cells. Vitamin D and/or Vitamin D receptor deficiency results in the impaired development of inkt cells. Vitamin D is critical very early during development of the immune system. Low levels of Vitamin D in utero resulted in significantly reduced numbers of inkt cells that failed to recover when calcitriol was used to supplement neonatal or adult mice. The data suggest that one of the consequences of early Vitamin D deficiency is a reduction in the numbers of inkt cells that develop. The inkt cells are required for the beneficial effects of calcitriol in eae. The important role of Vitamin D on inkt cells could impact the development of human immune-mediated diseases including multiple sclerosis and asthma.

Clinical Applications of Vitamin D

Teriparatide for Joint Erosions in Rheumatoid Arthritis: The TERA Trial (TERA)

Trial ID – NCT01400516

The investigators propose a randomized controlled open label study of teriparatide in the arm of men or women with rheumatoid arthritis and joint erosions. Specifically, the investigators will examine whether teriparatide in combination with a biologic can retard the development of joint erosions.

Baseline characteristics of the treatment groups were well balanced. After 52 weeks, the median change in erosion volume in the teriparatide group was -0.4 mm^3 (interquartile range [IQR] -34.5, 29.6) and did not differ significantly from that in controls (median change +9.1 mm^3 [IQR -29.6, 26.4]) (P = 0.28). No significant difference in change in erosion volume was noted at the radius, ulna, or metacarpophalangeal joints. Bone mineral density improved at the femoral neck and lumbar spine in the teriparatide group.

Treatment of Hypovitaminosis D in Rheumatoid Arthritis

Trial ID – NCT00423358

This study recruits' individuals with rheumatoid arthritis (RA) and low vitamin D concentrations. Subjects are dosed with vitamin D or placebo for one year. Primary outcome is change in bone turnover markers, additionally, bone mineral density and parameters of RA status are evaluated throughout the study.

Vitamin D3 in Systemic Lupus Erythematosus

Trial ID – NCT00710021

The study will last approximately 12 weeks and consist of three treatment groups: 1.) Participants will receive vitamin D3 2000 IU daily 2.) Participants will receive vitamin D3 4000 IU daily 3.) Participants will receive a vitamin D3 placebo daily. There will be four study visits for each participant. Visits will occur at screening, study entry, and Weeks 6 and 12. Physical examination, vital signs, and blood and urine tests will occur at all visits. For females of childbearing potential, a pregnancy test will be performed at screening and Week.

Baseline characteristics of the patients in the 3 treatment groups (placebo, low-dose vitamin D3, or

high-dose vitamin D3) were similar. Repletion of 25(OH)D (i.e., levels ≥30 ng/ml) was not observed in any of the patients who were receiving placebo, while repletion was observed in 16 of 33 patients receiving vitamin D3. The percentage of patients with an IFN signature response did not differ among the treatment groups. Moreover, there was no difference in the percentage of patients with an IFN signature response between those who remained vitamin D deficient and those who demonstrated repletion of vitamin D. Modular microarray analysis of a subset of patients (n = 40) did not reveal changes from baseline in any modules (including the IFN-inducible module) in any of the treatment groups, and no differences in expression were found between patients who demonstrated vitamin D repletion and patients who were persistently vitamin D deficient. Vitamin D3 was well tolerated, and there were no safety concerns.

Vitamin D3 Treatment in Pediatric Systemic Lupus Erythematosus

Trial ID – NCT01709474

The primary objective of this study is to evaluate the effects of 18 weeks of high-dose vitamin D3 supplementation compared with standard-dose vitamin D3 supplementation on immune function, glucose homeostasis, and bone metabolism in children with systemic lupus erythematosus (SLE) and serum 25-hydroxyvitamin D [25(OH)D] levels ≤20 ng/mL.

Discussion

- Our findings indicate that teriparatide treatment for 1 year does not significantly reduce erosion volume in the hands or wrists of patients with established RA with disease activity controlled by TNFi treatment.
- Vitamin D3 supplementation up to 4,000 IU daily was safe and well-tolerated but failed to diminish the IFN signature in vitamin D-deficient SLE patients. Higher 25(OH)D levels sustained for a longer duration may be required to affect immunologic outcomes.

Therapeutic applications of Vitamin B derivatives[11-46]

Oral vitamin B12 Replacement for the Treatment of Pernicious Anemia

Catherine Qiu Hua Chan1 *, Lian Leng Low1,2* and Kheng Hock Lee1,2

The objective of this review is to provide an update on the effectiveness of oral vitamin B12 for the treatment of pernicious anemia, the recommended dosage, and the required frequency of laboratory test and clinical monitoring. Relevant articles were identified by PubMed search from January 1, 1980 to March 31, 2016 and through hand search of relevant reference articles. Two randomized controlled trials, three prospective papers, one systematic review, and three clinical reviews fulfilled our inclusion criteria. We found that oral vitamin B12 replacement at 1000 μg daily was adequate to replace vitamin B12 levels in patients with pernicious anemia. We conclude that oral vitamin B12 is an effective alternative to vitamin B12 IM injections. Patients should be offered this alternative after an informed discussion on the advantages and disadvantages of both treatment options.

METHODS: Bibliographic search, Eligibility criteria and excluded studies

Clinical trial: B vitamins improve health in patients with coeliac disease living on a gluten free diet C.

HALLERT* SVENSSON, J. THOLSTRUP & B. HULTBERG§

BACKGROUND: Patients with coeliac disease living on a gluten free diet show vitamin deficiency and reduced subjective health status.

AIM: To study the biochemical and clinical effects of B vitamin supplementation in adults with longstanding coeliac disease (Autoimmune disorder).

METHODS: In a double blind placebo controlled multicenter trial, 65 coeliac patients (61% women) aged 45–64 years on a strict gluten free diet for several years were randomized to a daily dose of 0.8 mg folic acid,0.5 mg cyanocobalamin and 3 mg pyridoxine or placebo for 6 months. The outcome measures were psychological general wellbeing (PGWB) and the plasma total homocysteine (tHcy) level, marker of B vitamin status.

RESULTS: Fiftyseven patients (88%) completed the trial. The tHcy level was baseline median 11.7 lmol/ L (7.4–23.0), significantly higher than in matched population controls [10.2 lmol/ L (6.7–22.6) ($P < 0.01$)]. Following vitamin supplementation, tHcy dropped a median of 34% ($P < 0.001$), accompanied by significant improvement in wellbeing ($P < 0.01$), notably Anxiety ($P < 0.05$) and Depressed Mood ($P < 0.05$) for patients with poor wellbeing.

CONCLUSIONS: Adults with longstanding coeliac disease taking extra B vitamins for 6 months showed normalized tHcy and significant improvement in general wellbeing, suggesting that B vitamins should be considered in people advised to follow a gluten free diet.

High dose thiamine improves fatigue in multiple sclerosis

Antonio Costantini, Agostino Nappo, Maria Immacolata Pala, Antonietta Zappone

SUMMARY: Most of the patients with multiple sclerosis (MS) experience fatigue. Some observations indicate that fatigue and related manifestations concomitant with MS could be associated with an intracellular mild thiamine deficiency. We recruited 15 patients with MS who also experience fatigue and assessed the severity of the fatigue using the Fatigue Severity Scale. Although blood thiamine and thiamine pyrophosphate levels were within normal limits in all the patients, high dose thiamine therapy administered orally or parenterally led to an appreciable improvement of the fatigue. The absence of apparent decrease in blood thiamine despite the presence of symptoms referable to a mild thiamine deficiency suggests that these patients may have a dysfunction of the mechanisms of intracellular transport or structural enzymatic abnormalities. The administration of large quantities of thiamine was effective in reversing the fatigue in MS, suggesting that the abnormalities in thiamine dependent processes could be overcome by diffusion mediated transport at supranormal thiamine concentrations.

Vitamin B12, demyelination, remyelination and repair in multiple sclerosis

Ariel Millera, T, Maya Korema, Ronit Almogb, Yanina Galboiza

Multiple Sclerosis (MS) and vitamin B12 deficiency share common inflammatory and neurodegenerative pathophysiological characteristics. Due to similarities in the clinical presentations and MRI findings, the differential diagnosis between vitamin B12 deficiency and MS may be difficult. Additionally, low or decreased levels of vitamin B12 have been demonstrated in MS patients. Moreover, recent studies suggest that vitamin B12, in addition to its known role as a co-factor in myelin formation, has important immunomodulatory and neurotrophic effects. These observations raise the questions of possible relationship between the two disorders, and suggest further studies

of the need to close monitoring of vitamin B12 levels as well as the potential requirement for supplementation of vitamin B12 alone or in combination with the immunotherapies for MS patients. Elevated vitamin B12 levels in autoimmune lymphoproliferative syndrome attributable to elevated haptocorrin in lymphocytes

Objective: Identify the etiology of elevated B12 in autoimmune lymphoproliferative syndrome (ALPS).

Design: Peripheral blood of ALPS patients with elevated B12 and controls were evaluated.

Results: Total and holo haptocorrin (HC) levels were 26 and 23-fold higher in ALPS patients, respectively. No abnormal B12 Binding proteins were found. Western blot revealed HC in lymphocyte lysates only from ALPS patients.

Conclusion: Elevated concentrations of B12 found in ALPS patients were due to increased lymphocyte expression of HC.

Selective Vitamin B 12 Malabsorption in Adult Coeliac Disease Report on Three Cases with Associated Autoimmune Diseases

G. STENE LARSEN, J. MOSVOLD & B. LY Medical Dept., Lovisenberg Hospital, and Medical Dept., Aker Hospital, Oslo, Noway

Three cases of adult coeliac disease with severe vitamin BI2 deficiency not accompanied by folate or iron depletion are presented. Two of the patients had the extremely rare combination of coeliac disease and lack of intrinsic factor and autoimmune thrombocytopenic purpura. A close association between coeliac disease and autoimmunity is indicated by the development of autoimmune thyroiditis in the third patient. Vitamin B2 malabsorption caused by coeliac disease is emphasized as a pathogenetic mechanism of megaloblastic anaemia.

Thiamine and Fatigue in Inflammatory Bowel Diseases: An Openlabel Pilot Study

Antonio Costantini, MD,1,2 and Maria Immacolata Pala

Objectives: To demonstrate that fatigue and other disorders related to ulcerative colitis and Crohn's disease are the manifestation of an intracellular mild thiamine deficiency and not due to malabsorbtion, augmented requirements, or nutritional factors, and that this dysfunction is curable with high doses of thiamine administered orally or parenterally.

Design: In this pilot study, we treated fatigue in eight patients with ulcerative colitis and four patients affected by Crohn's disease from January to April 2011. Fatigue was measured using the chronic fatigue syndrome scale, and the determination of thiamine and thiamine pyrophosphate levels in the blood was carried out through blood tests. The levels of thiamine and thiamine pyrophosphate in the blood were normal. All patients were assigned to receive high doses of thiamine orally. Depending upon the body weight of each patient, dosage ranged from 600 mg/day (60 kg) to 1,500 mg/day (90 kg). The chronic fatigue syndrome scale as well as thiamine and thiamine pyrophosphate levels in the blood were measured 20 days after the beginning of the therapy.

Results: Ten patients out of twelve showed complete regression of fatigue, while the remaining two patients showed nearly complete regression of fatigue compared to the chronic fatigue syndrome scale scores before therapy.

Conclusions: The absence of blood thiamine deficiency and the efficacy of high dose thiamine in our patients suggest that fatigue is the manifestation of a thiamine deficiency, likely due to a dysfunction of the active transport of thiamine inside the cells, or due to structural enzymatic abnormalities. The administration of large quantities of thiamine increases the

concentration in the blood to levels in which the passive transport restores the normal glucose metabolism in all cells and leads to a complete regression of fatigue.

Pharmacokinetics and pharmacodynamics of MD1003 (high dose biotin) in the treatment of progressive multiple sclerosis

Laure Peyro Saint Paula, Danièle De Bruyne, Delphine Bernardc , Donald M. Mockd and Gilles L. Defere,f

Multiple sclerosis (MS) is a chronic, potentially highly disabling neurological disorder. No disease modifying treatments are approved in the progressive and not active forms of the disease. High doses of biotin were tested in an open label pilot study involving 23 patients with progressive MS and reported positive results. A randomized, doubleblind, placebo-controlled trial in 154 progressive MS patients confirmed the beneficial effect of MD1003 (high dose biotin) on reversing or stabilizing disability progression, with a good safety profile. It is proposed that MD1003 in progressive MS 1) increases energy production in demyelinated axons and/or 2) enhances myelin synthesis in oligodendrocytes. Biotin is highly bioavailable; absorption and excretion are rapid. The major route of elimination is urinary excretion. A high oral dose of biotin seems generally well tolerated but a few important safety concerns were identified: 1) teratogenicity in one species and 2) interference with some biotin-based laboratory immunoassays. Results of randomized, placebo-controlled trial are reassuring and provide hope for the treatment of progressive MS.

Update on riboflavin and multiple sclerosis: a systematic review

Mahshid Naghashpour 1, 2, Sima Jafarirad 2, 3, Reza Amani 4, 5*, Alireza Sarkaki 6, Ahmad Saedisomeolia 7, 8

Here, we systematically reviewed the literature concerning the health benefits of riboflavin on MS. The literature recorded within four main databases, including relevant clinical trials, experimental, and case control studies from 1976 to 2017 were considered. Both human and animal studies were included for review, with no restrictions on age, gender, or ethnicity. Experimental studies demonstrated that riboflavin deficiency triggers neurologic abnormalities related to peripheral neuropathies such as demyelinating neuropathy. Moreover, randomized controlled trials and case control studies in which MS patients received riboflavin supplementation or had higher dietary riboflavin intake showed improvements in neurological motor disability. Riboflavin is a cofactor of xanthine oxidase and its deficiency exacerbates low uric acid caused by high copper levels, leading to myelin degeneration. The vitamin additionally plays a significant role in the normal functioning of glutathione reductase as an antioxidant enzyme, and conditions of riboflavin deficiency lead to oxidative damage. Riboflavin promotes the gene and protein levels of brain derived neurotrophic factor (BDNF) in the CNS of an animal model of MS, suggesting that BDNF mediates the beneficial effect of riboflavin on neurological motor disability. Research to date generally supports the role of riboflavin in MS outcomes. However, further observational and interventional studies on human populations are warranted to validate the effects of riboflavin.

Methods: Search strategy, inclusion and exclusion criteria

Vitamin B6 supplementation improves proinflammatory responses in patients with rheumatoid arthritis

SC Huang1, JCC Wei2, DJ Wu3 and YC Huang1

The purpose of this study was to investigate whether vitamin B6 supplementation had a beneficial effect on inflammatory and immune responses in patients with rheumatoid arthritis (RA).). Patients with RA were under chronic inflammatory conditions, which may

possibly increase the use and metabolic turnover of plasma PLP. It was hypothesized therefore that supplementation of vitamin B6 would suppress inflammatory responses in patients with RA, but proinflammatory cytokine production was not affected. The non-effect result might have been due to the lower dose (50 mg/day) and short treatment period (30 days) used in Chiang et al.'s study. We thus postulated that a high dose of vitamin B6 supplementation (100 mg/day) and longer treatment period (12 weeks) would likely decrease the inflammatory responses of patients with RA 100 mg/day of vitamin B6 supplementation suppressed proinflammatory cytokines in patients with RA. Our results provide valuable reference data for clinical practice about the potential beneficial use of vitamin B6 to suppress inflammatory response in RA patients. A large dose of vitamin B6 supplementation (100 mg/day) suppressed proinflammatory cytokines in patients with RA.

Effects of B Vitamins in Patients with Multiple Sclerosis

S.P. Kalarn, Ronald Ross Watson

The aim here is to establish the correlation between vitamin B and Multiple Sclerosis. Although there have not been any significant results from clinical trials, there could be a causal role discovered if more research is done to understand the intricate pathway of vitamin B9 in neurodegeneration. Vitamin B12 has been shown to be needed to create the myelin sheaths that insulate the axons in the brain—the same structures that are attacked in patients with multiple sclerosis. Vitamin B12 deficiency has also been linked to neurodegeneration and inflammation in patients without multiple sclerosis. The Japanese research team concluded that massive dose methyl vitamin B12 therapy provided some therapeutic benefit to motor function related to vision and hearing. The combination therapy of vitamin B12 with lofepramine, and l phenylalanine also showed small therapeutic benefit in motor function. This shows that it is possible that vitamin B12 therapy could be used as a supplemental therapeutic in combination with other treatments to give patients with multiple sclerosis the best possible outcome. Although the other two research teams discussed did not find any correlation between vitamin B12 and multiple sclerosis, they proposed the idea of tHcy metabolism related to neuroinflammation. There is still much research to be done to assess the potential benefits of vitamin B12 therapy before a conclusion can be made, but at this time vitamin B12 therapy alone is not considered an effective therapy for multiple sclerosis.

Pyridoxal 5'phosphate (PLP) deficiency might contribute to the onset of type I diabetes

B.Rubi

Type I diabetes is preceded by autoimmunity to islet antigens, among them the protein glutamic acid decarboxylase, GAD65. Pyridoxal 5'phosphate (PLP) is formed from vitamin B6 by the action of pyridoxal kinase. Interaction of GAD65 with PLP is necessary for GAD65 mediated synthesis of the neurotransmitter aminobutyric acid (GABA). PLP is also a required cofactor for dopamine synthesis by Aromatic decarboxylase (LAADC). Both GAD65 and LAADC are expressed in pancreatic islets. Here it is proposed that lowering of PLP levels may contribute to the onset of type I diabetes. It is known that lack of vitamin B6, precursor of PLP, is linked to numerous abnormalities. Among them, studies have demonstrated that vitamin B6 intake and blood PLP levels are inversely associated with the risk of colorectal cancer. Hence the lack of the vitamin B6 derivative pyridoxal 5'phosphate might contribute to the appearance of pancreatic islet autoimmunity and type I diabetes onset.

Improvement of Vitiligo after Oral Treatment with VitaminB12 and Folic Acid and the Importance of Sun Exposure

LENNART JUHLIN and MATS J. OLSSON

The aim of this study is to test the hypothesis that folic acid, vitamin B12 and sun exposure could be helpful in treating vitiligo. One hundred patients with vitiligo were treated with oral folic acid and vitamin B12 after being informed that sun exposure might enhance their depigmentation. They were requested to keep record of sun exposure in summer and UVB radiation in winter. The minimal treatment time was 36 months but should be longer if improvement was achieved. The spread of vitiligo stopped in 64% of the patients after treatment. Folic acid and Vitamin B12 supplementation combined with sun exposure can induce depigmentation better than either the vitamins or sun exposure alone. Treatment should continue if the white areas continue to depigment. Further studies are needed to determine ideal minimal dosages of vitamins and UV exposure, as well as treatment time.

Therapeutic applications of astaxanthin[47-90]

Introduction

Astaxanthin (astaxanthin) (3,3'-dihydroxy-β, β'-carotene-4,4'-dione), a xanthophyll carotenoid , has been reported to exhibit multiple biological activities including modulation of os and inflammation through free radical quenching and activation of endogenous antioxidant systems via modulation of gene expression and has numerous advantages compared to some other carotenoids. Due to its unique structure, astaxanthin is incorporated in the lipid bilayer of cellular membranes, without damaging it, and prevents lipid-based oxidation. Moreover, its bioactivity is by far higher than other carotenoids such as α-carotene, β-carotene, and α-tocopherol. It has therefore attracted considerable interest because of its potential pharmacological effects including antidiabetic, anti-inflammatory, and antioxidant activities properties and anti-inflammatory; antidiabetic; as well as its neuro-, nephro-, and retinoprotective and cardiovascular effects.

Anti-inflammatory effects of astaxanthin in the human gingival keratinocyte line ndusd-1

Oral lichen planus is a chronic inflammatory disease that affects the mucous membrane of the oral cavity that can contribute to the development of other diseases. Inflammation in oral planus is a t-cell mediated autoimmune disease that acts through cytotoxic cd8+ t cells trigger apoptosis of keratinocytes.

In cytokine assay, il-6 production of the pre-astaxanthin group was decreased significantly ($p<0.05$) from 24 to 120h compared with that of the control group. Although the difference was not significant, tnf-alpha production in the pre-astaxanthin group was decreased as compared to the control group. Tnf-alpha production of the post-astaxanthin group was decreased significantly ($p<0.05$) for 1 and 12h compared with that of the control group. il-6 production in the post- astaxanthin group was decreased compared with that in the control group, although the difference was not significant. 1l-1 beta production was below the detection limit level for all groups.

In cell proliferation assay, the cell proliferation of the pre-astaxanthin group was increased significantly ($p<0.05$) from 1 to 12h compared with that of the control group. Proliferation was also significantly increased in the post-astaxanthin group($p<0.01$) from 12 to 120h compared with that of the control group.

Discussion on the mechanism of astaxanthin

The chemical structure of astaxanthin is c40h5204 and it contains two hydroxy groups and two carbonyl groups. Therefore, astaxanthin is functionalized on the surface of the cell membrane and the intracellular membrane. Also, it is reported that astaxanthin does not change the structure of the cell membrane. Maintenance of the cell membrane structure is useful for prevention and treatment of various diseases by protecting the cell from damage caused by oxidative stress such as ros and inflammatory simulation.

Protective effects of astaxanthin on cona - induced autoimmune hepatitis by the jnk/p-jnk pathway - mediated inhibition of autophagy and apoptosis

Hepatitis is a condition characterized by inflammation of the liver and the presence of inflammatory cells in the liver tissue. Autoimmune hepatitis is a chronic disease caused by abnormal immune response against liver cells. The incidence of severe autoimmune hepatitis that develops into liver cirrhosis, liver failure or even death has dramatically increased in many countries.

Results

- Liver injury in mice was alleviated by pretreatment with astaxanthin.
- Astaxanthin does not affect liver function or the inflammatory response.
- Astaxanthin pretreatment protected the liver from the damage caused by inflammation factors.
- Astaxanthin down regulated autophagy and apoptosis in cona- induced hepatitis by blocking pro-apoptotic protein bax and caspase-9.
- Astaxanthin attenuates jnk signal pathway by blocking the interaction between tnf-alpha and traf2.
- Astaxanthin protected the proliferation of primary hepatocytes induced by tnf-alpha and inhibited their apoptosis.

Astaxanthin mediates inflammation biomarkers associated with arthritis in human cho ndrosarcoma cells induced with interleukin-1beta

Arthritis is a leading cause of disability among adults. Osteoarthritis and rheumatoid arthritis are the most common arthritic diseases that involve the progression deterioration and loss of articular cartilage leading to debilitating impairment of joint function. While the pathogenesis of both arthritis are different, they both are characterized by chondrocyte dysfunction leading to inflammation, activation of matrix degrading proteinases and ultimately articular cartilage degeneration. Il- 1beta, a potent pro-inflammatory cytokine released by synovial cells in vivo during inflammation, plays a key role in cartilage degradation by stimulating the production of matrix metalloproteinases in chondrocytes. Il-1beta stimulation also results in pro-inflammatory cytokines and inflammatory mediators, further its stimulation in chondrocytes leads to generation of cellular ros which results in oxidative stress leading to cellualr damage , apoptosis , protein oxidation , dna modification and lipid peroxidation.

Method and result

Sw-1353 human chondrosarcoma cells were preincubated with 0, 0.01, or 1.0 micro mol/l astaxanthin for 48h, and oxidative stress induced with 10ng/ml il-1beta overnight. Astaxanthin (1.0 micro mol/l) accumulated in sw-1353 cells in a time dependent manner.il-1beta alone supressed intracellular antioxidant activity, resulting in overproduction of ros , matrix metalloproteinase inflammatory cytokines and mediators.In contrast pre-

incubation with astaxanthin increased ($p<0.05$) glutathione peroxidase activity and decreased ($p<0.05$) ros, mmp-13, il-6 , tnf-alpha and inflammatory mediators. Pre-treatment with astaxanthin also down regulated transcriptional activation of nf-kb and activator protein-1, which play critical roles in downstream production of mmp, inflammatory cytokines and mediators. Astaxanthin protects against degenerative factors upregulated by il-1beta, likely by scavenging ros required for transcriptional activation.

Astaxanthin reduces demyelination and oligodendrocytes deadth in rat model of multiple sclerosis

The administration of ast reduced the oligodendrocyte damage and myelin sheet disruption in a rat model of ms. The basket behavioral test showed the improvement of muscle strength in the ast group compared with cpz and sham groups. Besides, the results of rt-pcr and ihc indicated the beneficial effects of ast in declining demyelination and oligodendrocyte deadth in a rat model of ms.

Astaxanthin, a xanthophyll carotenoid , prevents developement of dextran sulphate sodium -induced murine colitis

Inflammatory bowel disease is a term for two disorders which are chron's disease and ulcerative colitis that are characterized by chronic inflammation of the gi tract. In the gi tract, oxidative stress leads to damages of the mucosal barrier functions and induces bacterial infection , which in turn stimulates the immune and inflammatory response in inflammatory bowel disease. In murine colitis models, the absence of macrophages and neutrophils leads to a decrease in ros generation , reduces mucosal expression of proinflammatory cytokines and ameliorates intestinal inflammation and damage. Astaxanthin prevented the development of dss induced colitis via the direct suppression of nf-kbeta, ap-1 and mapk activation.

Astaxanthin pretreatment attenuates hepatic ischemia reperfusion - induced apoptosis and autophagy via the ros/mapk pathway in mice

Hepatic ischemia reperfusion injury generally occurs in hemorrhagic shock, liver transplantation and other medical conditions and is a pathophysiological process influencing liver function after hepatic resection and severe trauma. Ischemia reperfusion is a multifactorial process and included major oxidative stress induced by ischemia and hypoxia. The endothelial and the kupffer cells activated by oxidative stress can generate large number of ros through nadph in the membrane. Eventually ros damage liver cells by changing the permeability of the cell membrane, causing lipid peroxidation or directly increasing neutrophil microcirculation. In addition, cytokines such as tnf-alpha and il-6 , released by activated kupffer cells and aggregated neutrophils also play a key role in ir injury. Tnf-alpha promote swelling of the endothelial cells to activate ros , while il-6 can induce hepatocyte injury to produce c-reactive protein , alpha-trypsin and fibrinogen which are associated with the mapk family , and the p13k/akt and hmgb1 pathways. In hepatic ir, astaxanthin weakened phosphorylation of the mapk family and provided protection by scavenging ros and inactivating kupffer cells which release inflammatory factors. Mapk pathways activated by tnf-alpha and il-6 can not only activate caspase-8 but also phosphorylate bcl-2 to induce caspase-9 activation. Inactive bcl-2 released beclin-1 that enhanced autophagy.

Impact of astaxanthin of diabetic pathogenesis and chronic complications

Furthermore, astaxanthin improves glucose metabolism by increasing glycogen reserves in the

liver. It modulates the activity of metabolic enzymes such as hexokinase, pyruvate kinase, glucose-6-phosphatase , fructose-1,6-phosphatase , and glycogen phosphorylase. It also promotes the irs-p13k-akt pathway of insulin by decreasing serine phosphorylation of irs proteins. In stz induced diabetic rat, a well-known t1dm model , the treatment with astaxanthin (50mg/kg bw/day ; 18 days) , significantly decreased the levels of ages , ros , and lipid peroxidation in the liver of diabetic rats. These results suggested that the inhibitory effect of astaxanthin on diabetic-induced hepatic dysfunction could be linked to the blocking of age formation and further anti-inflammatory effect.

Inflammation is a determinant factor in the onset and development of t1dm, t2dm , and their complications. Immune cells involved in pancreatic beta cell destruction are activated through a variety of cytokines including ifn - gamma, tnf-alpha , and il-1beta. Chronic low level inflammation is feature of t2dm, and tnf-alpha , il-1,1l-6,il-10, and adipokines serve as links between inflammation and metabolism. Obese tissue is characterized by macrophage infiltration, which is an important siurce of inflammation and tnf-alpha production in the tissue. Astaxanthin supplementation induces macrophage phenotype switch by the decrease of pro-inflammatory m1 markers (cd11 and mcp-1) and the increase of anti-inflammatory m2 markers.

Clinical applications of Astaxanthin

Effect of astaxanthin supplementation on plasma malondialdehyde levels and nihss of stroke patients

Clinicaltrials.gov identifier: nct03945526

A total of 24 subjects, with 12 subjects in the intervention group and 12 subjects in the control group were taken. The interventional group was given astaxanthin supplementation dose of 2*8mg per day for 7 days while the control group was given placebo.

Though no results were posted in this study, the objective was to prove the hypothesis that astaxanthin given to acute ischemic stroke patients would significantly lower their plasma malondialedhyde as well as nihss score as compared to placebo supplemented control group.

Safety and pharmacokinetics of phaffia rhodozyma astaxanthin

Clinicaltrials.gov identifier: nct03807050

The aim of this study was to monitor the safety and tolerability of astaferm, an astaxanthin dietary supplement derived from the yeast phaffia rhodozyma. In a clinical research centre, 12 healthy male adults were given a single dose of astaferm in a single-centre , open-label, non-randomized , single-dose study. On the next morning after overnight fasting, pre-dosing plasma sampling was performed. Then the subjects were given fat balanced breakfast followed by a single dose of astaferm capsules which contained a dose of 50mg of astaxanthin derived from phaffia rhodozyma. Following dosing, blood sampling was performed for 24hrs in-house(2,4,6,8,10,12 &24 hrs post-dose) and ambulatory at 48,72 and 168hrs post-dose. Blood for antioxidant activity is also drawn. Till date no results were posted for this study.

Astaxanthin formulation bioavailability

Clinicaltrials.gov identifier: nct02397811

This study was conducted to evaluate the oral bioavailability of 6 different formulations of astaxanthin in a double-blind crossover study involving 12 subjects. The subjects were given a standardized meal and were then given any 1 of 6

different formulations of astaxanthin. The 6 different formulation doses of astaxanthin were:-

- Enteric coated softgel capsule containing 4mg astaxanthin, 3 softgels per dose
- Liposomal astaxanthin containing 4.5 mg astaxanthin per gram. 2.66gm per dose
- Standard softgel containing 4 mg of astaxanthin per softgel, 3 softgels per dose
- Astaxanthin water soluble emulsion containing 1% astaxanthin ,1.2gm per dose
- Astaxanthin water dispersible powder containing 3% astaxanthin, 0.4gm per dose
- Standard softgel with astaxanthin gel containing 4mg astaxanthin, 3 softgels per dose

Blood would be immediately collected before consuming the standardized meal and formulation (0 hr) and then again at 4, 8 ,10 and 24hrs post dose by a licensed phlebotomist. In between the blood draws, the subjects would be allowed to resume their normal diet and lifestyle. This process would be repeated six times for the entire subject population with 2-week washout periods between each pharmacokinetic run. Then the samples collected were analyzed by hplc to quantify the astaxanthin.

Oral astaxanthin and semen quality, fertilization and embryo development in assisted reproduction techniques procedures

Clinicaltrials.gov identifier: nct02310087

This double blind study was to conducted to determine the efficacy of astaxanthin combined with vitamin e towards sperm quality , fertilization and embryo development in assisted reproduction techniques. The tests subjects were divided into 2 groups. The first group would receive 16mg astaxanthin with 40mg vitamin e daily for a period of 3 months. The 2nd group would receive 4 tablets of placebo daily for a period of 3 months. In both the groups, the quality of sperm , dna fragmentation and mitochondrial membrane potential of semen before and after the dietary supplementation would be evaluated. In this assisted reproduction technique procedure the fertilization rate, the quality of embryos , pregnancy rates and miscarriage rates in 1st trimester would be compared between both of the above groups.

Lipid lowering effects of an astaxanthin supplement in volunteers with mild dyslipidaemia

Clinicaltrials.gov identifier: nct02343497

The test subjects would be divided into 2 groups. The 1st group would be provided astaxanthin supplementation from phaffia rhodozyma, 6mg in lipid capsules , 2 caps per day for a duration of 12 weeks. The second group would be receiving placebo supplementation in lipid capsules, 2 caps per day for a duration of 12 weeks. Then the different lipid levels of the test subjects would be analyzed. The main purpose of this study was to determine the efficacy of astaxanthin supplementation on triglyceride plasmatic concentrations in subjects with mild dyslipidemia.

Clinical trial of astaxanthin formulation with exercise in sarcopenia elderly

Clinicaltrials.gov identifier: nct03368872

Test subjects would be divided into 2 groups. The 1st group would be receiving astaxanthin formulation intake for 1 month followed by 3-month exercise training regimen with astaxanthin formulation intake. The 2nd group would be receiving placebo intake for 1 month followed by 3month exercise training with placebo intake. The primary objective of this trial was to compare the efficacy of astaxanthin with placebo

after one month alone and after an additional 3 months of exercise training on mitochondrial and and skeletal muscle function in elderly subjects with evidence of mitochondrial dysfunction or sarcopenia.

Effects of isoflavone combined with astaxanthin on skin aging

Clinicaltrials.gov identifier: nct02373111

The test subjects were divided into 2 groups. In case of the 1st group, each subject would be taking one active tablet per day for 24weeks. Each tablet contains isoflavone 27mg and astaxanthin 4mg. In case of the 2nd group, each subject would be taking one placebo tablet per day for 24weeks. The results would be then analyzed. This study was designed to take isoflavone combined with astaxanthin to maximize their anti-aging ability and objectively measure the effect of the mixtures on facial wrinkles, hydration and elasticity.

Astaxanthin, lycopene and d-alpha-tocopherol for the treatment of skin aging

Clinicaltrials.gov identifier: nct03460860

The subjects were to be divided into two groups. Arm 1 group were to be supplemented with astaxanthin(2mg), lycopene(1.8mg) and d-alpha-tocopherol (10iu) daily for a duration of 12 weeks. Arm 2 groups on the other side were supplemented with placebo daily for 12 weeks. The results were to be analyzed. The aim of this study was to determine the increase in hydration levels of the skin, decrease in atypical skin pigmentation , and reduction of signs of photoaging on consumption of astaxanthin , lycopene and d-alpha-tocopherol together.

Effect of an antioxidants mix on cognitive performance and wellbeing: the bacopa, lycopene , astaxanthin , vitamin b12

Clinicaltrials.gov identifier: nct03825042

The study was conducted on 80 test subjects. One group of the test subjects were given mixture of four bioactive compounds i.e. bacopa, lycopene , astaxanthin , vitamin b12 once a day for a period of 8 weeks. The other group was given placebo supplementation once a day for a period of 8 weeks. The results were then analyzed. The aim of the study was to evaluate the influence of the mixture of the four active compounds mentioned before on cognitive performance, mood state and well being in subjects greater than or equals to 60yrs with no evidence of cognitive dysfunction.

Therapeutic applications of lycopene[84-104]

Anti-inflammatory effect of lycopene on endotoxin - induced uveitis in rats

Uveitis is an intraocular inflammatory disorder that accounts for up to 10%-25% of legal blindness worldwide. It primarily affects the uvea, but may also involveadjacent structures such as the retina and the vitreous. Endotoxin-induced uveitis in rats, which mimics human idiopathic nonspecific acute uveitis, is an established model for evaluating the therapeutic efficacy of potential treatments , especially those that may prevent or stop ocular inflammation. Lipopolysaccaride, the main component of gram negative bacteria , generates an acute inflammatory response in endotoxin induced uveitis. Lipopolysaccaride is is recognized by membrane bound receptors, principally on the surface of the macrophages , and triggers the release of proinflammatory factors such as tnf-alpha , il-6, no ,

monocyte chemoattractant protein-1.. The inflammatory response to lps also induces oxidative stress. Eventually the initiated proinflammatory cascades result in the breakdown of the blood occular barrier and the infiltration of leukocytes into both anterior and posterior segments of the eye, which contributes to further progression of eiu. Infiltrating cell number, total protein concentration , and no, tnf-alpha , and il- 6 levels were significantly elevated in the aqueous humor of the vehicle +lps grouprats compared to the vehicle controls. Compared to the vehicle + lps group, lycopene pretreatment significantly reduced aqueous humor concentrations of oxidative stress markers , no , tnf-alpha , and il-6 . Inflammatory score was also reduced. Lycopene reduced the infiltrating cell count and protein concentration, but differences did not reach significance. Most lycopene effects were equivalent to dexamethazone.

Lycopene ameliorates diabetic - induced changes in erythrocyte osmotic fragility and lipid peroxidation in wistar rats

Diabetes mellitus is a complex metabolic disorder in the endocrine system characterized by abnormalities in insulin secretion or insulin action that leads to the progressive deterioration of glucose tolerance, which causes hyperglycemia . The two main categories of the disease, type 1 diabetes mellitus also called iddm and type 2 ,the niddm. It has been shown that people who have diabetes have higher level of free radicals, which can cause diabetic complications. Hyperglycemia is mediated in large part, by a state of enhanced oxidative stress, which results in excessive production of ros. These reactive oxygen species then cause both adverse structural and functional changes in tissues including rbcs. Oxidative stress, mediated mainly by hyperglycemia - induced generation of free radicals , contributes to the development and progression of diabetes mellitus and its related complications.The result showed that there was significantly lowered erythrocyte osmotic fragility in diabetic animals treated with lycopene when compared with diabetic control group. In addition, there was significantly reduced erythrocyte malondialdehyde concentration, an index of lipid peroxidation in diabetic treated groups when compared with diabetic control group.

Anti-inflammatory activity of lycopene isolated from chlorella marina on type 2 collagen induced arthritis in sprague dawley rats

The anti-arthritic effect of lycopene (cis and trans) from the algae chlorella marina (al) has been compared with lycopene (all-trans) from tomato(tl) and indomethacin (indo). Arthritis was developed in male sprague dowley rats by collagen and the following parameters were studied. The activity of the inflammatory marker enzymes like cox, lox and myeloperoxidase were found to be decreased on treatment with al when compared to tl and indo. Changes in erythrocyte sedimentation rate , wbc count , rbc count , hb, c- reactive protein , rheumatoid factor and celeuroplasmin levels observed in the blood of arthritic animals were brough back to normal by al when compared to tl and indo.histopathology of paw and joint tissues showed marked reduction in edema on supplementation of al. Thus these results indicate the potential beneficiary effect of algal lycopene on collagen induced arthritis in rats. therefore lycopene from c.marina would be recommended as a better natural source with increased activity and without side effects in the treatment of anti-inflammatory diseases. Lycopene partially reverses symptoms of diabetes in rats with streptozotocin- induced diabetesdiabetes is a severe disease caused by autoimmune destruction of pancreatic beta cells(type1) or insulin resistance (type 2). The concomitant hyperglycemia or hyperinsulinemia have serious detrimental health effects. Also diabetes is associated with disturbances in carbohydrate, protein , fat metabolism that occurs

secondary to an absolute or relative lack of insulin. Here in this research investigation, type 1 diabetes is induced by an stz injection . The mechanism by which stz brings about its diabetic state include destruction of pancreatic beta cells that makes cells less active, leading to poor sensitivity of insulin for glucose uptake by tissues.

Method and result

Lycopene at the dose of 2.5mg/kg bw per day was orally administered to stz-induced diabetic rats for a period of 7 days after onset of diabetes. At the same time, food water intake and bw change were recorded daily. Upon sacrifice, biochemical parameters , such as serum glucose , insulin , total cholestrol , triglyceride , alanine aminotransferase , and aspartate aminotransferase , were measured in all experimental groups. Administration of lycopene at the dose of 2.5mg/kg bw per day significantly reduced serum glucose , tc, tg, alt, and ast levels , and increased serum insulin levels , but there were no improvements in food water intake and bw changes parameters in lycopene treated diabetic rats. The results suggest that orally administered lycopene exhibits a potent hypoglycemic effect in stz-induced diabetic rats and that lycopene may be useful for the management of diabetic mellitus.

Serum lycopene is inversely associated with long-term all-cause mortality in individuals with rheumatoid arthritis(ra)

The mortality of participants was significantly lower in the third tertile group (46.4%, 95% ci:40.1-52.7) compared to the first tertile group (66.5%, 95% ci:60.4-72.6) and the second tertile group (60.0%, 95% ci:53.6-66.4%) among participants with ra. There was a significance survival difference between the third tertile group and the first tertile group (logrank p< =.0001). After adjusting for demographic and other risk factors, ra participants in the third tertile group had a significantly reduced hazard ratio of all-cause mortality (hr=0.631, 95% ci:0.433-0.918) compared to ra participants in the first tertile group.These findings from a nationally representative sample indicate that serum lycopene has a significant association with long term all-cause mortality in individuals with ra.

Effect of lycopene against gastroesophageal reflux disease

Treatment with lycopene evidenced sententious physiological protection when scrutinized for ph, acidity (total and free) , volume of gastric juices and esophagitis index. Lycopene further embarked diminishing effect on oxidative stress through synchronizing protein and lipid peroxidation along with regulating the enzymatic activity of sod and catalase. Lycopene also modified the levels of immunoregulatory cytokines i.e. inf-1beta and il-6 favourably.

Conclusion

Therefore, it was concluded that lycopene can impart momentous protection against experimental esophagitis by wrapping up the ros and through dual inhibition of the arachidonic acid pathway.

Systemic lycopene as an adjunct to non-surgical periodontal therapy in chronic periodontitis patient among gutka chewers: a clinical study

Periodontitis is an inflammatory condition representing the response of the periodontal tissues to lps derived from gram negative anaerobic bacteria. In pathogenesis of periodontal disease-free radicals and oxidative stress play a significant role.The crp level was significantly reduced between the control and the test group which proved that lycopene along with non-surgical periodontal therapy was effective in combating oxidative stress in the 3 rd month.

Lycopene in the management of oral submucous fibrosis

Oral submucous fibrosis (osf) is a potentially malignant disease that is insidious and chronic in nature affecting the entire oral cavity. A variety of etiologic factors including capsaicin, betel nut alkaloids, hypersensitivity, autoimmunity, genetic predisposition and chronic iron and vitamin b deficiency have been suggested by researchers , the most common of which is chewing areca nut. Excessive use of areca nut may cause fibrosis due to increased synthesis of collagen and induce the production of free radicals and ros species , which are responsible for high rate of oxidation or peroxidation of polyunsaturated fatty acids which effect essential constituents of cell membrane and might be involved in tumorigenesis. The ingredients of the areca nut induce excessive ros species which damages the cell structures, including lipids and membranes, proteins and nucleic acids.There was a significant increase in mouth opening of all the 3 groups. The results were statistically significant between group a and c and group b and c. Lycopene in combination with intralesional steriods and hyaluronidase, is highly efficacious in improving the mouth opening and reducing other symptoms in patients with oral submucous fibrosis.

Effect of lycopene on plasma glucose, insulin levels, oxidative stress, and body weights of streptozocin - induced diabetic rats

Diabetic mellitus is a chronic metabolic disorder. The most accepted cause of diabetes is the oxidative damage caused by free radicals. During diabetes, persistent hyperglycemia causes an increased production of free radicals, especially ros, for all tissues from glucose oxidation and protein glycosylation. Damage of cellular organelles and enzymes and an increase in lipid peroxidation can be caused by high levels of free radicals and the simultaneous decline of antioxidant defence mechanisms. It was found that diabetic related increase in the blood glucose levels was reduced by supplementation of lycopene over an 8-week period. Plasma no levels and brain tissue gsh levels were meaningfully reduced in the treatment group compared to the diabetic group. In the haemolysate samples, it was determined that treatment group's sod , cat , gsh-px activities significantly increased compared to the diabetic group. In the brain tissue homogenates, cat and sod activity did not show a significant change , whereas gsh-px activity was increased in the treatment group compared to the diabetic group. Sod, cat , gsh-px mrna transcription levels were suppressed in the diabetic group compared to the control, and this suppressionwas stopped and increases were significantly induced by supplementation of lycopene. Thus, the oxidative damage and low insulin levels associated with diabetes were ameliorated with the administration of lycopene.

Clinical applications of lycopene

Introduction

Lycopene is a dietary carotenoid present in tomatoes and other red fruits and vegetables such as watermelon and pink grapefruit. It has been reported that dietary intake of tomato and tomato-derived products can reduce the risks of chronic diseases and various cancers, especially prostate cancer. Lycopene is a potent antioxidant as well as an inhibitor of proinflammatory and prothrombotic factors, although the mechanisms for these additional activities have not been clarified. Lycopene was shown to inhibit formation of proinflammatory cytokines and chemokines in macrophages. The inherent antioxidant activity of lycopene may contribute to immune system modulation.

Docetaxel plus lycopene in castration resistant, chemotherapy- naive prostate cancer patients

Trial id: nct01882985

This phase 2 study was primarily conduced to evaluate the impact of giving docetaxel and lycopene supplements in treating patients with hormone related prostate cancer not previously treated with chemotherapy. The objectives of this phase 2 trials were: -

- To define the prostate specific antigen response rate in subjects treated with a combination of docetaxel and lycopene.
- To determine the safety and tolerability of lycopene in combination with docetaxel.
- To determine the effects of docetaxel + lycopene therapy on the functioning of igfr-i, selected biomarkers, and docetaxel blood levels in plasma and peripheral blood mononuclear cells.

The methology of the trial had patients receiving docetaxel iv over 1hr in day 2 and lycopene po once daily on days 1-21. Treatment was repeated every 21 days for atleast 4 courses in the absence of disease progression or unacceptable toxicity.

14.29 % of subjects suffered serious adverse effect. 64.29% of subjects had some adverse effects that were not too serious.

A clinical trial to study the effects of two drugs, lycopene and prednisolone in patients with oral lichen planus(olp)

Trial id: nct02587117

Oral lichen planus, which is t cell mediated autoimmune disorder is believed to be caused by increased ros and lipid peroxidation together with an imbalance in the antioxidant defence system. This trial was conducted to compare the efficacy of lycopene and prednilsolone in the management of oral lichen planus. The test subjects were divided into 2 groups, lycopene and prednilsolone group. The lycopene group subjects were administered 2 capsules of lycopene as a single dose in morning for 2 months. Each capsule contained 2 mg of lycopene. Follow up was done at baseline, 2^{nd} , 4^{th} , 6^{th} and 8^{th} weeks of therapy. The same methodology was applied to prednilsolone group except the dose the dose of each capsule. Each capsule of prednilsolone contained 20mg of prednilsolone and the test subjects were given 2 capsules of prednilsolone each day. The results were analyzed.

Effect of lycopene on high risk prostatic tissue

Trial id: nct01443026

This study was conducted to determine the efficacy of lycopene on treating abnormal prostrate tissue. One group of test subjects was given 30mg of lycopene per day for a priod of 6 months. Another group of test subject were given 30mg of placebo per day for a period of 6 months. Then the results of both were compared by biopsy.

Lycopene in treating patients undergoing radical prostatectomy for prostate cancer

Trial id: nct00450749

A randomized phase 2 trial was conducted. Part of the patients received placebo po qd for 4-7weeks. Part of the patients received low-dose lycopene po qd for 4-7 weeks. Part of the patients received high-dose lycopene po qd for 4-7weeks. The 3 groups then underwent radical prostatectomy.

Lycopene or omega-3 fatty nutritional supplements in treating patients with stage 1 or stage 2 prostate cancer

Trial id: nct00402285

This randomized clinical trial was done to compare the efficacy of lycopene as compared to omega-3 fatty acids or a placebo while treating patients with stage 1 or stage 2 prostate cancer. The 1st group of patients received 15g of oral lycopene twice daily. The 2nd group of patients received 1g of oral omega-3 fatty acids 3 times daily. The 3rd group received oral placebo daily. The treatment was continued for 90 days and then a biopsy was scheduled for those with absence of disease progression. Patients completed a dietary questionnaire at baseline and then for 3 days each month during study therapy. Quality of life was then assessed at baseline and at 3 months. Prostate tissue needle biopsies and blood samples were collected at baseline and at 3 months. Tissue and blood samples were then examined for lycopene and omega-3 fatty acids , omega 6-fatty acids, insulin like growth factor (igf)-1, igf binding protein - 5 , and cox-2 gene by pcr , cdna microarray hybridization , and other gene expression assays. No significant detection of individual genes associated with dietary intake and supplementation of lycopene and omega 3 fatty acid were observed.

Novel 13c carotenoids for absorption and metabolism studies in humans

Trial id: nct01692340

This study was conducted to compare the absorption and metabolism of 3 different compounds found in tomatoes i.e. phytoene, phytofluene and lycopene. The test subjects were divided into 3 groups. The isotopically labeled lycopene group received 10.2 mg of labeled carotenoid with a controlled meal. The isotopically labeled phytoene group received 3.2 mg of labeled carotenoid with a controlled meal. The isotopically labelled phytofluene received 10mg of labeled carotenoid with a controlled meal. After this, pharmacokinetic studies for absorption and metabolism were followed in each of the 3 groups. Although only differing from lycopene by 4 double bonds, phytoene exhibits markedly different kinetic characteristics in human plasma , providing insight into metabolic processes contributing to phytoene enrichment in plasma and tissues compared with lycopene.

II. CONCLUSION

Chemical and in vitro cell studies have shown preventive properties of these compounds, being a potent antioxidant, against a variety of ROS and RNS. In addition, the epidemiologic and immunopathological studies suggest that consumption of these compounds may lower multiple disease risk. Such potential benefits have been ascribed in part to high concentrations of compounds in nutraceutical treatments. However, these findings have yet only been supported by a small number of intervention trials. By defining the right population and combining antioxidant and immunopathological potentials of these compounds with vitamins and other bioactive plant compounds, the beneficial role of them in other diseases that could be better clarified in future studies.

III. REFERENCES

[1]. Cooper, J. D. et al. Inherited variation in vitamin D genes is associated with predisposition to autoimmune disease type 1 diabetes. Diabetes 60, (2011).

[2]. Wang, J. et al. Meta-analysis of the association between vitamin D and autoimmune thyroid disease. Nutrients vol. 7 (2015).

[3]. Wessels, I. & Rink, L. Micronutrients in autoimmune diseases: possible therapeutic benefits of zinc and vitamin D. Journal of Nutritional Biochemistry vol. 77 (2020).

[4]. Hayes, C. E. et al. Vitamin D actions on CD4+ T cells in autoimmune disease. Frontiers in Immunology vol. 6 (2015).

[5]. Smyk, D. S., Orfanidou, T., Invernizzi, P., Bogdanos, D. P. & Lenzi, M. Vitamin D in autoimmune liver disease. Clinics and Research in Hepatology and Gastroenterology vol. 37 (2013).

[6]. Van Belle, T. L., Gysemans, C. & Mathieu, C. Vitamin D in autoimmune, infectious and allergic diseases: A vital player? Best Practice and Research: Clinical Endocrinology and Metabolism vol. 25 (2011).

[7]. Agmon-Levin, N., Theodor, E., Segal, R. M. & Shoenfeld, Y. Vitamin D in systemic and organ-specific autoimmune diseases. Clin. Rev. Allergy Immunol. 45, (2013).

[8]. Baeke, F., Gysemans, C., Korf, H. & Mathieu, C. Vitamin D insufficiency: Implications for the immune system. Pediatric Nephrology vol. 25 (2010).

[9]. Harrison, S. R., Li, D., Jeffery, L. E., Raza, K. & Hewison, M. Vitamin D, Autoimmune Disease and Rheumatoid Arthritis. Calcified Tissue International vol. 106 (2020).

[10]. Cantorna, M. T., Zhao, J. & Yang, L. Vitamin D, invariant natural killer T-cells and experimental autoimmune disease. in Proceedings of the Nutrition Society vol. 71 (2012).

[11]. Demirkaya, S. et al. Malondialdehyde, glutathione peroxidase and superoxide dismutase in peripheral blood erythrocytes of patients with acute cerebral ischemia. Eur. J. Neurol. (2001) doi:10.1046/j.1468-1331.2001.00166.x.

[12]. Gariballa, S. E. & Sinclair, A. J. Assessment and treatment of nutritional status in stroke patients. Postgraduate Medical Journal (1998) doi:10.1136/pgmj.74.873.395.

[13]. Hussein, G. et al. Antihypertensive and neuroprotective effects of astaxanthin in experimental animals. Biol. Pharm. Bull. (2005) doi:10.1248/bpb.28.47.

[14]. Palozza, P. & Krinsky, N. I. Astaxanthin and canthaxanthin are potent antioxidants in a membrane model. Arch. Biochem. Biophys. (1992) doi:10.1016/0003-9861(92)90675-M.

[15]. Shen, H. et al. Astaxanthin reduces ischemic brain injury in adult rats. FASEB J. (2009) doi:10.1096/fj.08-123281.

[16]. Barber, P. A., Demchuk, A. M., Hirt, L. & Buchan, A. M. Biochemistry of ischemic stroke. Advances in neurology (2003) doi:10.1002/chin.200331291.

[17]. Comhaire, F. H., El Garem, Y., Mahmoud, A., Eertmans, F. & Schoonjans, F. Combined conventional/antioxidant 'Astaxanthin' treatment for male infertility: A double blind, randomized trial. Asian J. Androl. (2005) doi:10.1111/j.1745-7262.2005.00047.x.

[18]. Marchetti, C., Obert, G., Deffosez, A., Formstecher, P. & Marchetti, P. Study of mitochondrial membrane potential, reactive oxygen species, DNA fragmentation and cell viability by flow cytometry in human sperm. Hum. Reprod. (2002) doi:10.1093/humrep/17.5.1257.

[19]. Virro, M. R., Larson-Cook, K. L. & Evenson, D. P. Sperm chromatin structure assay (SCSA®) parameters are related to fertilization, blastocyst development, and ongoing pregnancy in in vitro fertilization and intracytoplasmic sperm injection cycles. Fertil. Steril. (2004) doi:10.1016/j.fertnstert.2003.09.063.

[20]. Chemes, H. E. & Rawe, V. Y. Sperm pathology: A step beyond descriptive morphology. Origin, characterization and fertility potential of abnormal sperm phenotypes in infertile men.

Human Reproduction Update (2003) doi:10.1093/humupd/dmg034.

[21]. Franco, J. G. et al. Significance of large nuclear vacuoles in human spermatozoa: Implications for ICSI. Reprod. Biomed. Online (2008) doi:10.1016/S1472-6483(10)60291-X.

[22]. Higuera-Ciapara, I., Félix-Valenzuela, L. & Goycoolea, F. M. Astaxanthin: A review of its chemistry and applications. Critical Reviews in Food Science and Nutrition (2006) doi:10.1080/10408690590957188.

[23]. Agarwal, A., Nallella, K. P., Allamaneni, S. S. R. & Said, T. M. Role of antioxidants in treatment of male infertility: An overview of the literature. Reproductive BioMedicine Online (2004) doi:10.1016/S1472-6483(10)61641-0.

[24]. Yuan, J. P., Peng, J., Yin, K. & Wang, J. H. Potential health-promoting effects of astaxanthin: A high-value carotenoid mostly from microalgae. Molecular Nutrition and Food Research (2011) doi:10.1002/mnfr.201000414.

[25]. Imamovic Kumalic, S. & Pinter, B. Review of clinical trials on effects of oral antioxidants on basic semen and other parameters in idiopathic Oligoasthenoteratozoospermia. Biomed Res. Int. (2014) doi:10.1155/2014/426951.

[26]. NCT03460860. Nno: no outcome of interest Astaxanthin (2 mg) + Lycopene (1.8 mg) + D-Alpha-Tocopherol (10 IU) For The Treatment Of Skin Aging. https://clinicaltrials.gov/show/NCT03460860 (2018).

[27]. NCT02373111. Effects of Isoflavone Combined With Astaxanthin on Skin Aging. https://clinicaltrials.gov/show/NCT02373111 (2015).

[28]. NCT03368872. Clinical Trial of Astaxanthin Formulation With Exercise in Sarcopenia Elderly. https://clinicaltrials.gov/show/NCT03368872 (2017).

[29]. NCT02343497. Lipid-lowering Effects of an Astaxanthin Supplement in Volunteers With Mild Dyslipidaemia. https://clinicaltrials.gov/show/NCT02343497 (2015).

[30]. NCT02397811. Astaxanthin Formulation Bioavailability. https://clinicaltrials.gov/show/NCT02397811 (2015).

[31]. Li, J. et al. Protective effects of astaxanthin on conainduced autoimmune hepatitis by the JNK/p-JNK pathway-mediated inhibition of autophagy and apoptosis. PLoS One (2015) doi:10.1371/journal.pone.0120440.

[32]. Li, J. et al. Astaxanthin pretreatment attenuates hepatic ischemia reperfusion-induced apoptosis and autophagy via the ROS/MAPK pathway in mice. Mar. Drugs (2015) doi:10.3390/md13063368.

[33]. Landon, R. et al. Impact of Astaxanthin on Diabetes Pathogenesis and Chronic Complications. Marine Drugs (2020) doi:10.3390/md18070357.

[34]. Sakai, S. et al. Astaxanthin, a xanthophyll carotenoid, prevents development of dextran sulphate sodiuminduced murine colitis. J. Clin. Biochem. Nutr. (2019) doi:10.3164/jcbn.1847.

[35]. Sakai, S. et al. Astaxanthin, a xanthophyll carotenoid, prevents development of dextran sulphate sodium-induced murine colitis. J. Clin. Biochem. Nutr. (2019) doi:10.3164/jcbn.18-47.

[36]. Lotfi, A., Soleimani, M. & Ghasemi, N. Astaxanthin reduces demyelination and oligodendrocytes death in a rat model of multiple sclerosis. Cell J. (2021) doi:10.22074/cellj.2021.6999.

[37]. Kimble, L., Mathison, B. & Chew, B. Astaxanthin Mediates Inflammation Biomarkers Associated with Arthritis in Human Chondrosarcoma Cells Induced with

Interleukin-1β. Am. J. Adv. Food Sci. Technol. (2013) doi:10.7726/ajafst.2013.1004.

[38]. Lindsey, K., Bridget, M. & Boon, C. Astaxanthin Mediates Inflammation Biomarkers Associated with Arthritis in Human Chondrosarcoma Cells Induced with Interleukin-1β. Am. J. Adv. Food Sci. Technol. (2013) doi:10.7726/ajafst.2013.1005.

[39]. Miyachi, M., Matsuno, T., Asano, K. & Mataga, I. Anti-inflammatory effects of astaxanthin in the human gingival keratinocyte line NDUSD-1. J. Clin. Biochem. Nutr. (2015) doi:10.3164/jcbn.14-109.

[40]. Juhlin, L. & Olsson, M. J. Improvement of vitiligo after oral treatment with vitamin B12 and folic acid and the importance of sun exposure. Acta Derm. Venereol. 77, (1997).

[41]. Rubí, B. Pyridoxal 5'-phosphate (PLP) deficiency might contribute to the onset of type I diabetes. Med. Hypotheses 78, (2012).

[42]. KASTRUP, W., MOBACKEN, H., STOCKBRÜGGER, R., SWOLIN, B. & WESTIN, J. Malabsorption of Vitamin B12 in Dermatitis Herpetiformis and Its Association with Pernicious Anaemia. Acta Med. Scand. 220, (1986).

[43]. Kalarn, S. P. & Watson, R. R. Effects of B Vitamins in Patients with Multiple Sclerosis. in Nutrition and Lifestyle in Neurological Autoimmune Diseases: Multiple Sclerosis (2017). doi:10.1016/B978-0-12-805298-3.00026-8.

[44]. Huang, S. C., Wei, J. C. C., Wu, D. J. & Huang, Y. C. Vitamin B6 supplementation improves pro-inflammatory responses in patients with rheumatoid arthritis. Eur. J. Clin. Nutr. 64, (2010).

[45]. Tourbah, A. et al. MD1003 (high-dose biotin) for the treatment of progressive multiple sclerosis: A randomised, double-blind, placebo-controlled study. Mult. Scler. 22, (2016).

[46]. Costantini, A. & Pala, M. I. Thiamine and fatigue in inflammatory bowel diseases: An open-label pilot study. J. Altern. Complement. Med. 19, (2013).

[47]. Chan, C. Q. H., Low, L. L. & Lee, K. H. Oral Vitamin B12 replacement for the treatment of Pernicious Anemia. Frontiers in Medicine vol. 3 (2016).

[48]. Naghashpour, M., Jafarirad, S., Amani, R., Sarkaki, A. & Saedisomeolia, A. Update on riboflavin and multiple sclerosis: A systematic review. Iranian Journal of Basic Medical Sciences vol. 20 (2017).

[49]. Miller, A., Korem, M., Almog, R. & Galboiz, Y. Vitamin B12, demyelination, remyelination and repair in multiple sclerosis. in Journal of the Neurological Sciences vol. 233 (2005).

[50]. Costantini, A., Nappo, A., Pala, M. I. & Zappone, A. High dose thiamine improves fatigue in multiple sclerosis. BMJ Case Rep. (2013) doi:10.1136/bcr-2013-009144.

[51]. Kwatra, B. A REVIEW ON POTENTIAL PROPERTIES AND THERAPEUTIC APPLICATIONS OF GRAPE SEED EXTRACT. World J. Pharm. Res. 9, 2519–2540 (2020).

[52]. Kwatra, B. A REVIEW ON POTENTIAL PROPERTIES AND THERAPEUTIC APPLICATIONS OF BRANCHED CHAIN AMINO. WORLD J. Pharm. Pharm. Sci. 9, 561–588 (2020).

[53]. Kwatra, B. & Arora, C. The Studying Of Movements Resonant the Pendulum Elastic. Indian J. Appl. Res. 10, 1–2 (2020).

[54]. Kwatra, B. COLLAGEN SUPPLEMENTATION : THERAPY FOR SKIN DISORDERS : A REVIEW. World J. Pharm. Res. 9, 2504–2518 (2020).

[55]. Kwatra, B. A REVIEW ON POTENTIAL PROPERTIES AND THERAPEUTIC APPLICATIONS OF LYCOPENE. Int. J. Med. Biomed. Stud. 4, 33–44 (2020).

[56]. Kwatra, B. & Mudgil, M. LIGHT ASSISTED TIO2-BASED NANOCOMPOSITE SYSTEMS: A NOVEL TREATMENT FOR CANCER. Int. J. Med. Biomed. Stud. 4, 28–32 (2020).

[57]. Kwatra, B. A Review on Potential Properties and Therapeutic Applications of Vitamin D. Int. J. Sci. Res. 9, 682–691 (2020).

[58]. Kwatra, B. HYDROQUINONE: A novel growth inhibitor and apoptosis inducer in U-251 MG CELLS. Int. J. Med. Biomed. Stud. 3, 15–16 (2019).

[59]. Kwatra, B. HACKING THE BLOOD-BRAIN BARRIER. Eur. J. Biol. Med. Sci. Res. 5, 10–13 (2017).

[60]. Kwatra, B. EXPRESSION AND CHARACTERIZATION IN PICHIA PASTORIS BY CLONING OF DELTA 4 DESATURASE FROM ISOCHRYSIS GALBANA. Indian J. Appl. Res. 9, 1–2 (2019).

[61]. Kwatra, B. CALCIUM AND IRON ABSORPTION: INVITRO STUDIES. Int. J. Med. Biomed. Stud. 3, 59–61 (2019).

[62]. Kwatra, B. Allicin-An After Digestion Antimicrobial Agent. ACTA Sci. Microbiol. 2, 48–51 (2019).

[63]. Kwatra, B. LOCATOR THEORY FOR ELE-MENTS IN PERIODIC TABLE 'LEPT'. Glob. J. Pure Appl. Chem. Res. 5, 9–10 (2017).

[64]. Kwatra, B. & Agarwal, R. Misfolded Proteins in Parkinson ' s and Alzheimer Disease : A Review Misfolded Proteins in Parkinson ' s and Alzheimer Disease : A Review. Int. J. Sci. Res. Sci. Technol. 7, 57–74 (2020).

[65]. Kwatra, B. & A, A. UTERINE CANCER: SEX DOMINANT CHARACTER. Int. J. Adv. Res. 08, 663–667 (2020).

[66]. Kwatra, B. Studies on People Employed in High Risk Workplace : Between Genetic Polymorphism for Tumor Necrosis Factor (TNF- A) and Blood Pressure. Int. J. Innov. Res. Technol. 6, 268–270 (2020).

[67]. Kwatra, B. & Arora, C. Investigation of Conductance Quantization with Magnetic Field Control and Application of Biosensor. Int. J. Innov. Res. Technol. 6, 271–272 (2020).

[68]. Kwatra, B. Candidate genes of OCD interacts with human retrovirus to form new link in inflammatory hypothesis. Int. J. Sci. Appl. Res. 7, 1–2 (2020).

[69]. Kwatra, B. COLLAGEN SUPPLEMENTATION : THERAPY FOR THE PREVENTION AND TREATMENT OF OSTEOPOROSIS AND OSTEOARTHRITIS : A REVIEW. WORLD J. Pharm. Pharm. Sci. 9, 589–604 (2020).

[70]. Kwatra, B. & Arora, C. THE UNEXPLAINED SIMILARITY BETWEEN THE ATOMIC AND GRAVITATIONAL MODELS. Int. J. Adv. Res. 8, 1099–1107 (2020).

[71]. Kwatra, B. A Review on Potential Properties and Therapeutic Applications of DHA and EPA. ijppr.humanjournals 16, 140–176 (2019).

[72]. Kwatra, B. Tinospora Crispa As A Future Cure For Obesity/Cholesterol. Int. J. Sci. Technol. Res. 6, 340–341 (2017).

[73]. Bharat Kwatra. Procuring Natural Dye for Solar Cell Using Leaf Waste. Int. J. Sci. Eng. Res. 7, 46–47 (2019).

[74]. Kwatra, B. THE SIMVASTATIN AND DMXAA ON THE CO-CULTURE OF B16.F10 MELANOMA CELLS AND MACROPHAGES SHOWS ANTITUMOR ACTIVITY. World J. Pharm. Res. 8, 1318–1319 (2019).

[75]. Kwatra, B. Bioactive-Compounds: alternative to control Candida spp. Int. J. Sci. Res. Rev. 8, 221–223 (2019).

[76]. Kwatra, B. Effects of Mineral Separation by Time and Enteric Coating Mechanism for Calcium and Iron Absorption in Mammalia. Int. J. Sci. Res. 8, 1265–1270 (2019).

[77]. Kwatra, B. Maprovit 3, 6, 9: Perfect Companion of your Immune System to Fight Corona Virus Hit. Int. J. Sci. Res. 9, 241–241 (2020).

[78]. Kwatra, B. & Mudgil, M. Untangling the Mathematical Relation Between Natural Selection and Adaptive Radiation Using Macromolecules and Microevolutionary Forces. Int. J. Sci. Res. Sci. Technol. IJSRST | 7, 313–339 (2020).

[79]. Chaitanya Arora1, B. K. Mathematical and Statistical Approach to Define Past Present Future Events. Int. J. Sci. Res. 8, 261–263 (2019).

[80]. Kwatra, B. MECHANISMS OF PATTERN FORMATION OF FBP17 IN MAST CELLS. Int. J. Adv. Res. 7, 413–414 (2019).

[81]. Mudgil1, M. & Kwatra2, B. Mosquito Menace Aim: Observing the life cycle of Aedes aegypti mosquito and understanding its behavior towards different natural oils for encouraging natural methods of repellence. Int. J. Sci. Res. 8, 1314–1315 (2019).

[82]. Kwatra, B. A REVIEW ON POTENTIAL PROPERTIES AND THERAPEUTIC APPLICATIONS OF BROMELAIN. www.wjpps.com 8, 488–500 (2019).

[83]. Kwatra, B. Holothuroidea (Sea Cucumber): Key to Anti-Aging. Int. J. Sci. Res. 8, 884–884 (2019).

[84]. Kwatra, B. & Mudgil, M. PROTONATED CRAB SHELL WASTE AS FUNGAL INHIBITOR. Int. J. Med. Biomed. Stud. 3, 111–116 (2019).

[85]. Magbanua, M. J. M. et al. Physical activity and prostate gene expression in men with low-risk prostate cancer. Cancer Causes Control (2014) doi:10.1007/s10552-014-0354-x.

[86]. Magbanua, M. J. M. et al. Gene expression and biological pathways in tissue of men with prostate cancer in a randomized clinical trial of lycopene and fish oil supplementation. PLoS One (2011) doi:10.1371/journal.pone.0024004.

[87]. Moran, N. E. et al. Compartmental and noncompartmental modeling of 13C-lycopene absorption, isomerization, and distribution kinetics in healthy adults. Am. J. Clin. Nutr. (2015) doi:10.3945/ajcn.114.103143.

[88]. Moran, N. E. et al. Absorption and distribution kinetics of the 13c-labeled tomato carotenoid phytoene in healthy adults. J. Nutr. (2016) doi:10.3945/jn.115.220525.

[89]. Bostwick, D. G. et al. Independent origin of multiple foci of prostatic intraepithelial neoplasia: Comparison with matched foci of prostate carcinoma. Cancer (1998) doi:10.1002/(SICI)1097-0142(19981101)83:9<1995::AID-CNCR16>3.0.CO;2-2.

[90]. Giovannucci, E. et al. Intake of carotenoids and retino in relation to risk of prostate cancer. J. Natl. Cancer Inst. (1995) doi:10.1093/jnci/87.23.1767.

[91]. Jain, M. G., Hislop, G. T., Howe, G. R. & Ghadirian, P. Plant foods, antioxidants, and prostate cancer risk: Findings from case, control studies in Canada. Nutr. Cancer (1999) doi:10.1207/S15327914NC3402_8.

[92]. Giovannucci, E. Tomatoes, tomato-based products, lycopene, and cancer: Review of the epidemiologic literature. Journal of the National Cancer Institute (1999) doi:10.1093/jnci/91.4.317.

[93]. Pastori, M., Pfander, H., Boscoboinik, D. & Azzi, A. Lycopene in association with α-tocopherol inhibits at physiological concentrations proliferation of prostate carcinoma cells. Biochem. Biophys. Res. Commun. (1998) doi:10.1006/bbrc.1998.9351.

[94]. Clinton, S. K. et al. cis-trans lycopene isomers, carotenoids, and retinol in the human prostate. Cancer Epidemiol. Biomarkers Prev. (1996).

[95]. NCT00402285. Lycopene or Omega-3 Fatty Acid Nutritional Supplements in Treating Patients With Stage I or Stage II Prostate Cancer.

https://clinicaltrials.gov/show/NCT00402285 (2006).

[96]. NCT00450749. Lycopene in Treating Patients Undergoing Radical Prostatectomy for Prostate Cancer. https://clinicaltrials.gov/show/NCT00450749 (2007).

[97]. Han, G. M. & Han, X. F. Serum lycopene is inversely associated with long-term all-cause mortality in individuals with rheumatoid arthritis: Result from the NHANES III. Eur. J. Integr. Med. (2016) doi:10.1016/j.eujim.2015.10.003.

[98]. Aydin, M. & Çelik, S. Effects of lycopene on plasma glucose, insulin levels, oxidative stress, and body weights of streptozotocin-induced diabetic rats. Turkish J. Med. Sci. (2012) doi:10.3906/sag-1202-44.

[99]. Kumar, A., Bagewadi, A., Keluskar, V. & Singh, M. Efficacy of lycopene in the management of oral submucous fibrosis. Oral Surgery, Oral Med. Oral Pathol. Oral Radiol. Endodontology (2007) doi:10.1016/j.tripleo.2006.07.011.

[100]. Giri, A. K., Rawat, J. K., Singh, M., Gautam, S. & Kaithwas, G. Effect of lycopene against gastroesophageal reflux disease in experimental animals. BMC Complement. Altern. Med. (2015) doi:10.1186/s12906-015-0631-6.

[101]. Bayramoglu, A., Bayramoglu, G. & Senturk, H. Lycopene partially reverses symptoms of diabetes in rats with streptozotocin-induced diabetes. J. Med. Food (2013) doi:10.1089/jmf.2012.2277.

[102]. Renju, G. L., Kurup, G. M. & Kumari, C. H. S. Anti-inflammatory activity of lycopene isolated from Chlorella marina on Type II Collagen induced arthritis in Sprague Dawley rats. Immunopharmacol. Immunotoxicol. (2013) doi:10.3109/08923973.2012.742534.

[103]. Eze, E. D. et al. Lycopene Ameliorates Diabetic-Induced Changes in Erythrocyte Osmotic Fragility and Lipid Peroxidation in Wistar Rats. J. Diabetes Mellit. (2017) doi:10.4236/jdm.2017.73006.

[104]. Goncu, T. et al. Anti-inflammatory effect of lycopene on endotoxin-induced uveitis in rats. Arq. Bras. Oftalmol. (2016) doi:10.5935/0004-2749.20160102.

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