Supplementation for Health, Wellness and Control

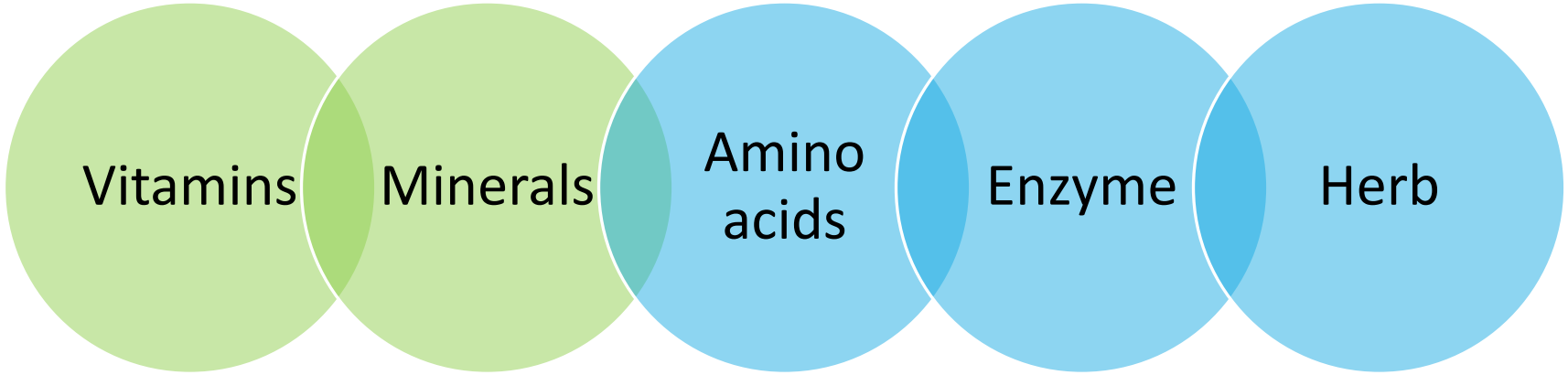
Prepared by: M. Williams
May 2018

Objectives

1. To establish the role of supplements for the prevention and management of NCDs (HTN & T2DM)
2. To identify key micronutrients/supplements and their role in the prevention and management of T2DM and HTN
3. To outline common drug-nutrient/disease-nutrient interactions with micronutrients
4. To summarize using case examples the effects of drug-nutrient and nutrient-disease interactions in T2DM and HTN

Dietary Supplements

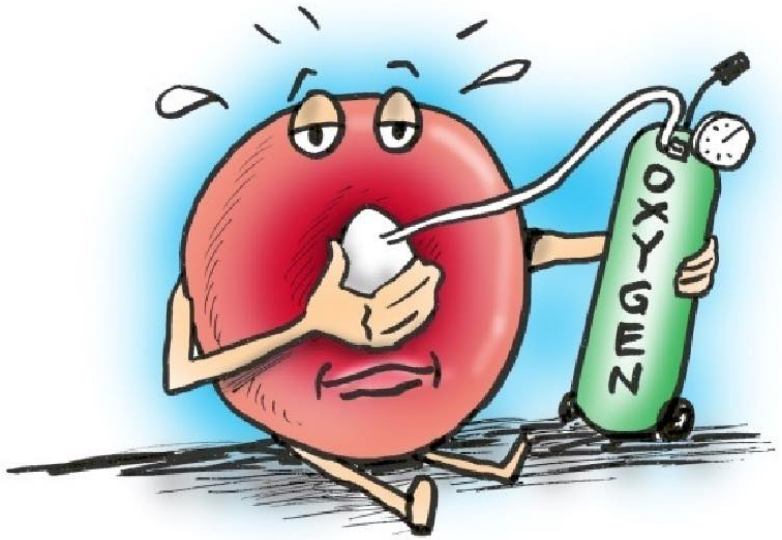
Dietary supplements are products designed to augment your daily intake of nutrients.



Benefits of Supplements in NCDs

- Anti-oxidative
- Support physiological processes
- Combat Nutrient Deficiencies

Anti-oxidative Micronutrients and NCDs



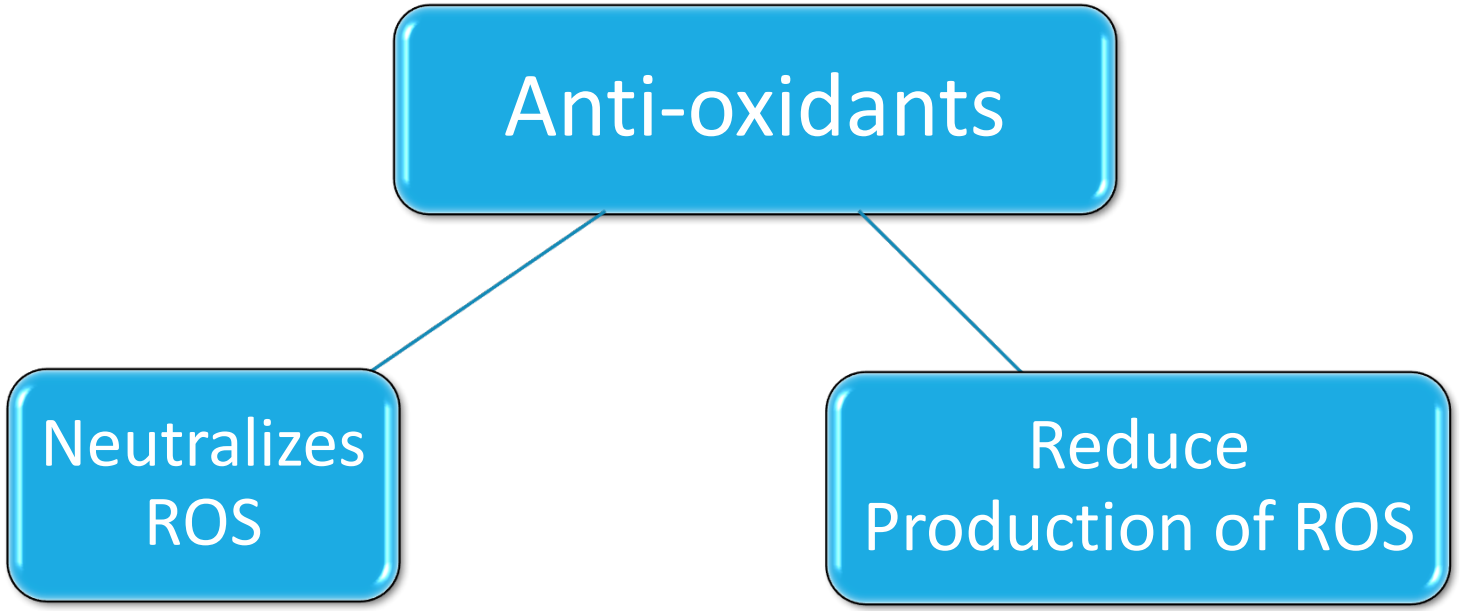
- Human beings need oxygen to survive
- Utilization of oxygen produces ROS
- Free radicals overtime results in degenerative Cellular function
- Development of Non-Communicable Diseases (NCDs)

Anti-oxidative Micronutrients and NCDs

- Excessive production of reactive oxygen species is reflected by increased peroxidation of lipid and DNA, leading to oxidative stress.
- Free radicals are also produced from exposure to cigarette smoke, excess exposure to the sun, drinking alcohol, exposure to large amounts of heavy metals and during any inflammatory response
- The reactive oxygen species (ROS) has now been identified to play a fundamental role in the pathogenesis of cellular function including endothelial dysfunction and atherosclerosis
- Glucose auto- oxidation, monocyte dysfunction and non-enzymatic glycation etc.

Anti-oxidative Micronutrients and NCDs

- Oxidative stress is currently suggested as the mechanism underlying all non-communicable diseases as chronic diseases with slower progression causing 38 million deaths per year globally, with rising prevalence across the world particularly in developing countries .

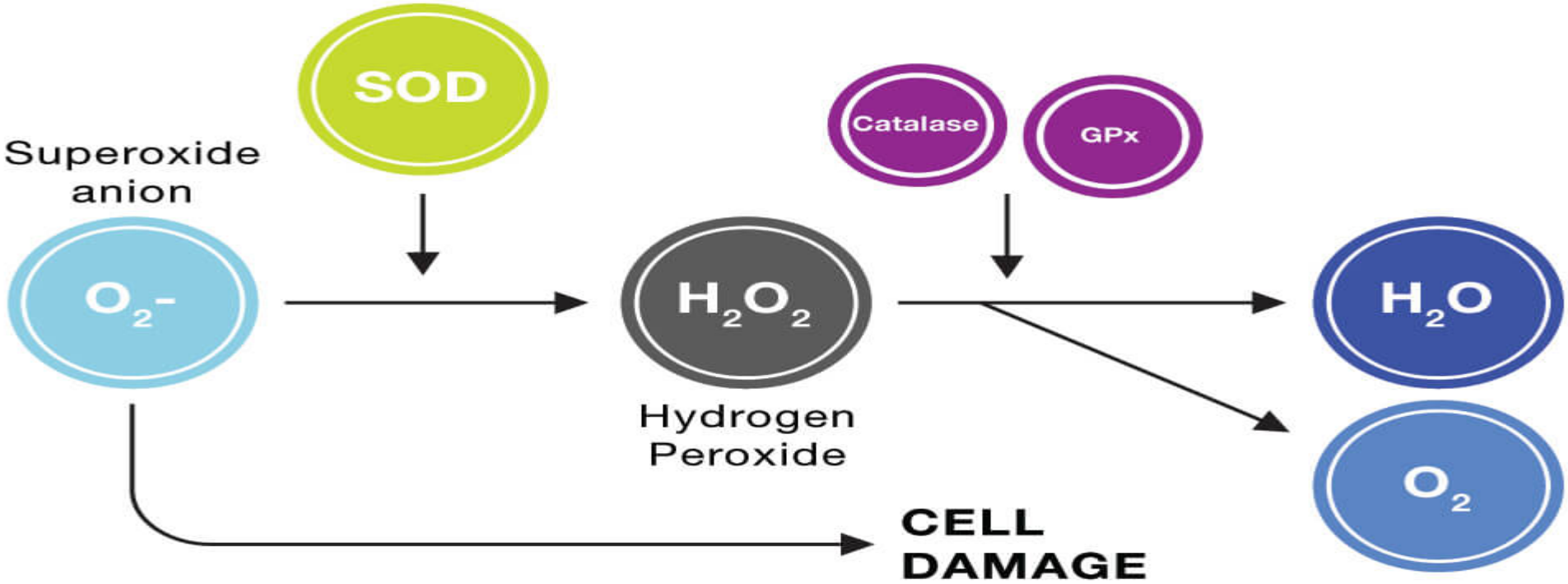


Evert, A.B. and Boucher, J.L. et al; Nutrition Therapy Recommendations For the Management of Adults with Diabetes,:Position Statement by the ADA, Diabetes Care 2013, 36;3821-42.
Franz, J et al; Evidence-based diabetes nutrition therapy recommendations are effective: the key is individualization. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy

Anti-oxidative Micronutrients and NCDs

- This antioxidant defence mechanism can be divided into two groups:

1. Anti-oxidative enzymes, present inside the cells such as superoxide dismutase; catalase and glutathione peroxidase which prevents formation of free radicals.



Evert, A.B. and Boucher, J.L. et al; Nutrition Therapy Recommendations For the Management of Adults with Diabetes,:Position Statement by the ADA, Diabetes Care 2013, 36;3821-42.
Franz, J et al; Evidence-based diabetes nutrition therapy recommendations are effective: the key is individualization. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2014:7 65–72

Anti-oxidative Micronutrients and NCDs

2. Certain vitamins and minerals and some specific phytochemicals have a major anti-oxidative effect in the body.

Vitamins

- Vitamin C
- Vitamin E

Minerals

- Selenium
- Zinc
- Copper

Phytochemicals

- Beta Carotene

Evert, A.B. and Boucher, J.L. et al; Nutrition Therapy Recommendations For the Management of Adults with Diabetes,:Position Statement by the ADA, Diabetes Care 2013, 36;3821-42.
Franz, J et al; Evidence-based diabetes nutrition therapy recommendations are effective: the key is individualization. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2014:7 65–72

Micronutrients Support Physiological Processes

- Vitamins and minerals function in the human body as metabolic regulators, influencing a number of physiological processes.

- All physiological processes within the body are directed or influenced by **ENZYMES**

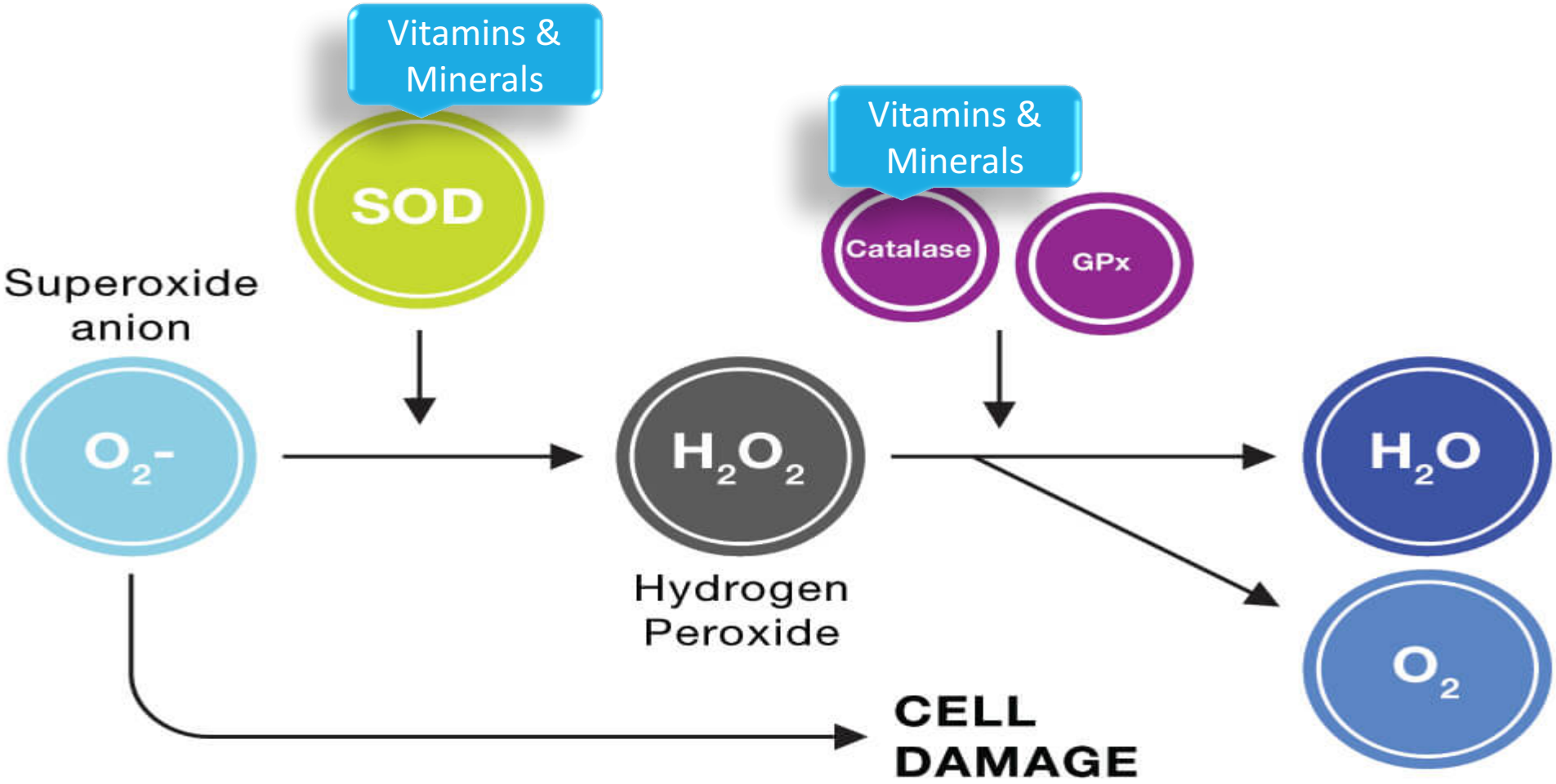
Micronutrients Support Physiological Processes

- The basic tasks of enzymes are to build up and break down various chemical compounds, usually proteins.

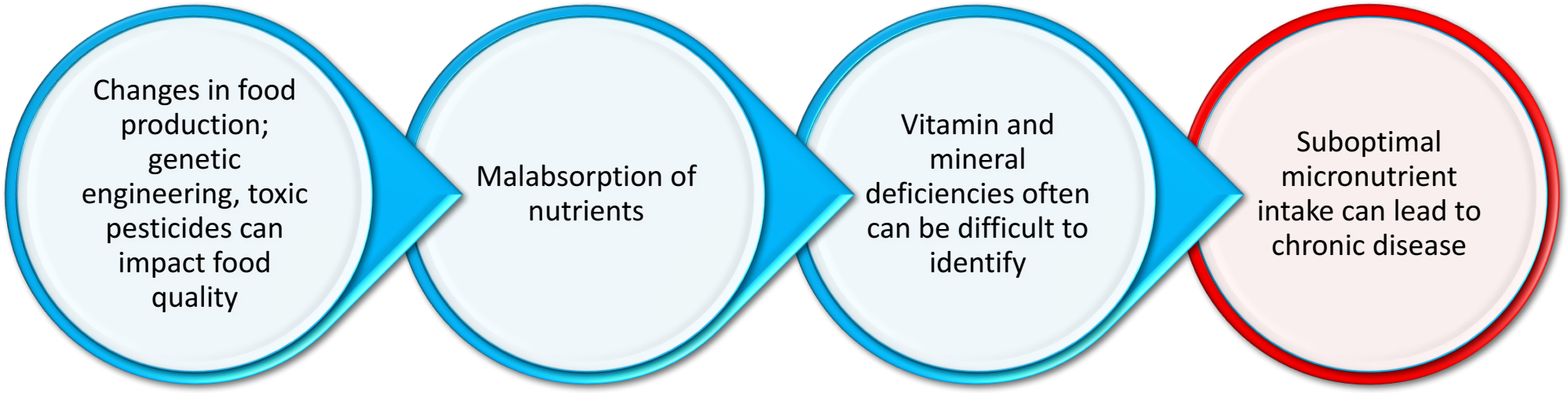
- Proteins form our:
  - Cell walls
  - Hormones
  - neurotransmitters etc

- Micronutrients are biological catalysts as they serve as co-factors or co-enzymes

Micronutrients Support Physiological Processes



Factors Leading to Nutrient Deficiencies



Common Nutrient Deficiencies

The most common nutrient deficiencies are:

- Vitamin D
- Omega-3s
- Magnesium
- Vitamins A, E and B12
- Iodine
- Calcium
- Iron
- Zinc

BMC Bioinformatics 2012; 13(Suppl 14): S10

Osteoporosis International September 2013: 24(9); 2499–2507

Dietary Supplements and Diabetes/HTN

Omega-3(ALA) – DM

- Antioxidant properties
- Promotes glucose uptake in muscles
- Increases sensitivity of the body to insulin
- Positive effect on diabetic neuropathy
- Helps with weight loss

S/E

Hypoglycaemia and decrease iron levels

Omega-3 (ALA) - HTN

- Antioxidant properties
- Has the potential to regulate blood pressure

S/E

May cause fluctuation in blood pressure control

Dietary Supplements and Diabetes/HTN

Omega-3 (EPA/DHA) Fatty acids - DM

- Increase levels of adiponectin
- Increases insulin sensitivity
- Decrease insulin resistance

Omega-3 Fatty acids –HTN

- Lower blood pressure
- Reduce triglycerides
- Slow the development of plaque in the arteries
- Reduce the chance of abnormal heart rhythm

RCTs found that Omega-3 decreases the risk of cardiovascular disease and events such as heart attack and stroke.

Are Omega-3 Fats Good for Diabetes?, Published September 27, 2017 by David Spero, BSN, RN

American Journal of Clinical Nutrition 2010 May;91(5):1255-60

Dietary Supplements and Diabetes/HTN

Coenzyme Q10 (Ubiquinone & Ubiquinol) - DM

- Helps cell make energy and acts as an antioxidant
- Improves heart health in people with diabetes

S/E

- Interacts negatively with blood thinners and blood pressure medications

Coenzyme Q10 (Ubiquinone & Ubiquinol) - HTN

- Blood pressure lowering properties

S/E

- Increases the hypertensive effects of anti-hypertensive medications.

Prevent Disease July 26, 2016

American Journal of Clinical Nutrition 2010 May;91(5):1255-60

Dietary Supplements and Diabetes/HTN

Zinc (Protamine)– DM

- Insulin homeostasis
- Reduce insulin resistance
- Prolongs the action and half life of insulin
- Promotes insulin secretion

S/E

- Hypoglycaemia

Zinc (Protamine) – HTN

- Positively impacts arterial blood pressure
- Zinc interacts with other minerals; especially copper to maintain blood pressure (8:1)

S/E

- Excess can cause hypertension by increasing oxidative stress on arteries

Granados-Silvestre MA et al. Minerals and diabetes, 2014;82:97-103

American Journal of Clinical Nutrition 2010 May;91(5):1255-60

Dietary Supplements and Diabetes/HTN

Magnesium – DM

- Needed co-factor for carrying out >300 enzymatic reactions, specifically in the processes of phosphorylation and, in general, in those where the use of transference of ATP is necessary
- Promotes uptake of insulin by cells and maintains vascular tone.
- Intracellular magnesium regulates the action of insulin

S/E

High levels can lead to irregular heart rate, muscle weakness, hypotension and difficulty breathing

Magnesium – HTN

ADA, 2016

- People receiving about 368 mg/day of magnesium for about three months had overall reductions in systolic blood pressure of 2.00 mm Hg and diastolic blood pressure of 1.78 mm Hg.
- Magnesium might only be effective among people with magnesium deficiency or insufficiency.

S/E

Hypotension

American Journal of Clinical Nutrition 2010 May;91(5):1255-60

NCCIH Ongoing Research

- Chromium effects on elevated blood glucose levels
- The use of Yoga on glucose control in people at risk for DM
- Ginko Biloba Extract on diabetes medications

American Journal of Clinical Nutrition 2010 May;91(5):1255-60

Nutrient-Drug/Disease Interactions

- Interaction is a consequence of physical, chemical or pathophysiologic relationship between a drug and nutrient

- Interactions can occur between a drug and a nutrient, multiple nutrients, dietary pattern or specific foods.

- An interaction is clinically significant if it alters the therapeutic drug response and or compromise nutritional status

Nutrient-Drug/Disease Interactions

- Supplements contain a large variety of micronutrients and phytochemicals that have been associated with health benefits.

- Most supplements however consist of complex phytochemicals that can inhibit or induce the activity of cytochrome P450 family of enzymes

Nutrient-Drug/Disease Interactions

- The **clinical significance** of any particular interaction depends on the **seriousness of the dose-related drug toxicity** and the extent to which the systemic drug concentration increases.

- The latter relies on multiple factors that include:
  - Bioavailability of the interacting drug
  - The concentration of the interacting nutrient
  - The vulnerability of the patient to the interaction

Bailey et al.CMAJ 2012. DOI:10.1503/cmaj.120951

Nutrient-Drug/Disease Interactions

- These interactions can result in decreased bioavailability of drug causing treatment failure or increased bioavailability causing toxicity and adverse effects.

- The patient’s nutritional status and dietary components with pharmacological activity can affect drug metabolism thereby altering action and function.

Nutrient-Drug/Disease Interactions

- Medications can play a significant role in developing nutrient deficiencies.
  - Drug induced micronutrient depletion may be responsible for the unexplained symptoms that affect medication compliance (for example zinc and ACE inhibitors/ARBs)
- Many micronutrients are potentially vulnerable to the effects of prescribed medicines when consumption is regular and sustained.

Nutrient-Drug/Disease Interactions

- Medications can affect nutrients by:
  - Decreasing food intake
  - Decrease nutrient absorption
  - Slowing down nutrient production
  - Interfering with nutrient metabolism
  - Increasing nutrient excretion

Common Drug-Nutrient/Disease Interactions – HTN/DM

Drug Category	Interaction/Outcome	Recommendations
Anti-hypertensives: ACE Inhibitors ARBs CCBs BBs Diuretics	ACE inhibitors and ARBs deplete zinc and increase potassium levels CCBs and Thiazide diuretics deplete potassium BBs deplete coenzyme Q10 and Vitamin B3	ACEIs/ARBs – **Zinc <30mg/day** CCBs/Thiazide diuretics – Potassium **<100mg/day** Beta Blockers – **CoQ10 100-200mg/day, Vit B3 – 16-18mg/day**

Common Drug-Nutrient/Disease Interactions – HTN/DM

Drug Category	Interaction/Outcome	Recommendations
Diuretics: Furosemide HCTZ Spiranolactone Acetazolamide	Loop and thiazide diuretics deplete; magnesium, potassium and zinc Potassium sparing diuretics deplete folic acid	Loop and Thiazide diuretics – **Magnesium 250mg/day** **Potassium <100mg/day** **Zinc <30mg/day** Potassium sparing diuretics: **Folic acid 400 mcg/day**

Common Drug-Nutrient/Disease Interactions – HTN/DM

Drug Category	Interaction/Outcome	Recommendations
Oral Hypoglycemics: Metformin Glimeperide Glipizide Pioglitazone Sitagliptin	Depletion of Folic acid and Vitamin B12	Vitamin B12 **– 25-400mcg/day** Folic acid **– 400mcg/day**
Insulin	Omega-3- synergism	Omega-3 **- <300 mg/day**

Case Activities

Case # 1

A 68-year-old diabetic woman visited the cardiology clinic with the chief complaint of palpitation at rest and with minimal exertion. She had a history of **type II diabetes mellitus** for around 9 years treated with Metformin 1500 mg/day, and Pioglitazone 45 mg/day.

Her other medications were as follows: Aspirin 81 mg/day, Atorvastatin 20 mg/day, Losartan 25 mg/day and Calcium + Vitamin D (500 mg+ 200 IU)/day.

Case # 1

On physical examination, she was to some extent pale with subicterus, otherwise unremarkable. 12-lead electrocardiography was normal while trans-thoracic echocardiography showed normal left and right ventricular size and global systolic function with mild to moderate mitral regurgitation and normal pulmonary arterial pressure.

Case # 1

Laboratory examination revealed severe macrocytic anaemia with hypochromia, anisocytosis and tear drop cells on peripheral blood smear table .

Thyroid and renal function tests were normal. She had neither neuropsychiatric nor gastro-entrologic symptoms.

She was not taking proton-pump inhibitors or other antacid medications either.

Case # 1

1. What is the suspected diagnosis?

Case # 1

1. What is the suspected diagnosis?

Ans: Megaloblastic anaemia related to Metformin-induced vitamin B12

- Competitive inhibition of calcium-dependent absorption in the ileum. Although calcium supplementation decreases the malabsorption, it does not increase serum vitamin B12 levels.

2. What other micronutrient/s would you be concerned about and why?

Case # 1

What other micronutrient/s would you be concerned about and why?

Ans: Zinc and Potassium

Losartan (ARB) has the potential to deplete zinc and increase potassium levels

Case # 2

A 65-year-old woman referred to the pharmacy clinic with the chief complaint of palpitation at rest and low blood pressure. She had a history of **hypertension** for around 6 years treated with an initial management of:

- HCTZ 12.5mg/day, Nifedipine 40mg/day then
- HCTZ 25mg/day + Nifedipine 40mg/day then
- Nifedipine 30mg/day+ Hctz 12.5mg + Losartan 75mg/day

With all the pharmacotherapy adjustments the patient's blood pressure was consistently unstable and compliance became a challenge for the patient.

Case # 2

With further investigation the patient informs the pharmacist at one refill of her medicines that she does not like taking prescription medicines and often time substitute them for herbal medicines.

The pharmacist advised the patient to stop that practice as this may affect her overall care.

Case # 2

The patient's daughter (a nursing student) did some research online and recommended the following supplements:

- Magnesium 500mg/day,
- Fish Oil 300mg/day and
- B complex

After approximately two months of taking the supplements along with the medications the patient noted very low blood pressure reading with high heart rates. She complaint of light headedness along with fatigue.

Note that the patient now takes Nifedipine 40mg/day + Losartan 50mg/day along with the supplements

Case # 2

1. What do you suspect is happening to this patient?

Case # 2

1. What do you suspect to the problem/problems with this patient?

Ans:

Non-Compliance to pharmacotherapy and concomitant use of herbal remedies with prescribed pharmacotherapy.

Daily allowance of Magnesium as a supplement is 250mg/day not exceeding 350mg/day. Above 350mg Magnesium can greatly lower blood pressure.

2. What other micronutrient/s would you be concerned about and why?

Case # 2

2. What other micronutrient/s would you be concerned about and why?

Potassium and Zinc – Thiazide diuretics, CCBs and ARBs increases the excretion of potassium and ARBs also depletes zinc.

Case # 3

A 55-year-old male was admitted in April 2011 after being found lying naked in the street talking to himself and cursing passers-by. He was taken to the hospital by his relatives.

Mental status examination on admission found that the patient was conscious but unable to answer questions correctly. He covered his head with a quilt during the examination for no obvious reason. He laughed to himself, manifested inappropriate emotions and appeared to lack insight into his condition. He had difficulty concentrating, had slowed reactions, and got a score of 20 on the Mini-Mental Status Exam (MMSE)—indicating moderate cognitive impairment.

Other symptoms included diarrhoea and scaly skin.

Case # 3

Given an admission diagnosis of Psychosis Not Otherwise Specified and was treated accordingly. After x 3/7 of treatment the patient cognitive function did not improve.

Upon further probing of his relatives they shared that the patient has heart and blood pressure problems for 7 years and was taking several medicines for that problem. Included in the patient's medication was a beta blocker.

Case # 3

What do you suspect is happening to this patient?

Case # 3

What do you suspect is happening to this patient?

Ans: Vitamin B-3 deficiency due to long term use of beta blocker

What is the name of the condition that is associated with Vitamin B-3 deficiency?

Case # 3

What is the name of the condition that is associated with Vitamin B-3 deficiency?

Pellagra – diarrhoea, dermatitis, mental disorder induced by Vitamin B-3 deficiency.

Conclusion

- Supplements such as micronutrients play an important role in metabolic and cellular processes.
- Their deficiency due to an increase clearance or deficiency in ingestion may contribute to secondary complications in chronic diseases such as HTN and DM
- Their administration as supplements are important to achieving health, wellness and control.
- Administration, however, should be carefully monitored to reach adequate doses in order to achieve the expected effects, avoiding reaching concentrations that may produce adverse effects.

References

Ali, M.K et al.; Achievement of Goals in US Diabetes Care: 1999-2010, N Engl J Med 2013;368:1613-24..

Evert, A.B. and Boucher, J.L. et al; Nutrition Therapy Recommendations For the Management of Adults with Diabetes,:Position Statement by the ADA, Diabetes Care 2013, 363821-42.

Standards of Medical Care in Diabetes-2013 Diabetes Care 2013;36(Suppl. 1):S11–S66

Evert, A.B. and Boucher, J.L. et al; Nutrition Therapy Recommendations For the Management of Adults with Diabetes,:Position Statement by the ADA, Diabetes Care 2013, 363821-42.

The Diabetes Control and Complications Trial Research Group , The Effect of Intensive Treatment of Diabetes on the Development and Progression of Long-Term Complications in Insulin-Dependent Diabetes Mellitus; New England Journal of Medicine 1993, 329(14):977-86.

Standards of Medical Care in Diabetes-2013 Diabetes Care 2013;36(Suppl. 1):S11–S66

Evert, A.B. and Boucher, J.L. et al; Nutrition Therapy Recommendations For the Management of Adults with Diabetes,:Position Statement by the ADA, Diabetes Care 2013, 36;3821-42.

Franz, J et al; Evidence-based diabetes nutrition therapy recommendations are effective: the key is individualization. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2014:7 65–72

Evert, A.B. and Boucher, J.L. et al; Nutrition Therapy Recommendations For the Management of Adults with Diabetes,:Position Statement by the ADA, Diabetes Care 2013, 36:3821-42...

Cozma AI, Sievenpiper JL, de Souza RJ,et al. Effect of fructose on glycemic control in diabetes: a systematic review and meta-analysis of controlled feeding trials. Diabetes Care 2012;35:1611–1620

Evert, A.B. and Boucher, J.L. et al; Nutrition Therapy Recommendations For the Management of Adults with Diabetes,:Position Statement by the ADA, Diabetes Care 2013, 36:3821-42..

Position of the Academy of Nutrition and Dietetics:Use of Nutritive and Nonnutritive SweetenersJ Acad Nutr Diet. 2012;112:739-758


THANK
YOU!