ANTIOXIDANTS & POLYPHENOLS

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OVERVIEW

- Antioxidants:
  - Antioxidants limit the action of free radicals
  - Exercise training improves antioxidant capacity
  - Little to no evidence for supplementation, consume as part of a well-balanced diet
  - ROS play an important role in adaptation to exercise

- Polyphenols:
  - Scavenge radicals
  - May provide protection through multiple mechanisms
  - More research is needed

ANTIOXIDANTS

What is an antioxidant?

Does it help exercise performance?

OXIDANTS

First, we need to understand what an oxidant is before we can understand antioxidants

What is an **OXIDANT**?

- Any atom/molecule that "**steals/accepts**" electrons from other molecules
- Molecules that promote oxidation

What is ***oxidation***?

- The removal of electrons

ROS & RNS

Reactive Oxygen Species (ROS):
"A form of oxygen or an oxygen rich molecule that acts as either a powerful oxidant or reductant."

Oxidants that contain oxygen (parent: superoxide)

Reactive Nitrogen Species (RNS):
Oxidants that contain nitrogen (parent: nitric oxide)

***NO** can be considered a reactive nitrogen or a reactive oxygen species but is generally referred to as a RNS.

$N \equiv {}^{\bullet}O$ or $N{=}O^{\bullet}$
NO or $NO^{\bullet}$

Other reactive N species:
$ONNO^-$, NO_2, $NO_2^{\bullet}$, etc.

Not very reactive except with metals.

Halliwell and Gutteridge. *Oxford University Press*. 2006

ANTIOXIDANT

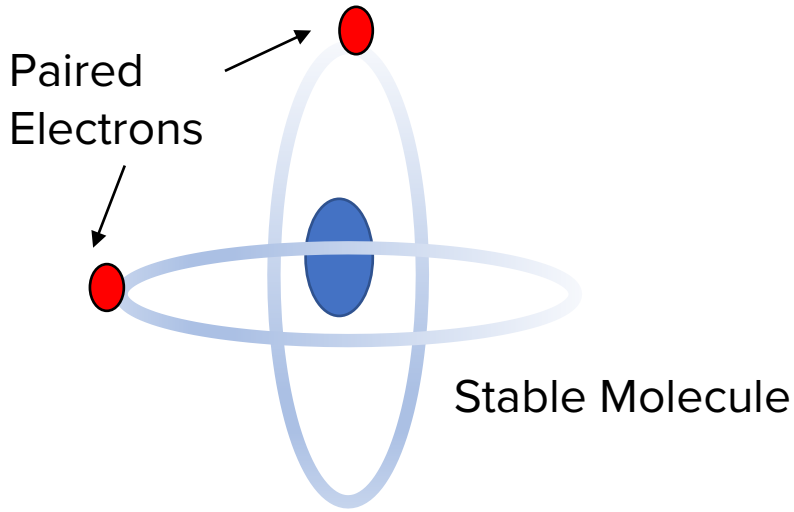
What is an Antioxidant?

"Substance that prevents or delays oxidation."

Anti-oxidants prevent or limit the actions of ***free radicals*** usually by removing their unpaired electron and thus converting them into something far less reactive.

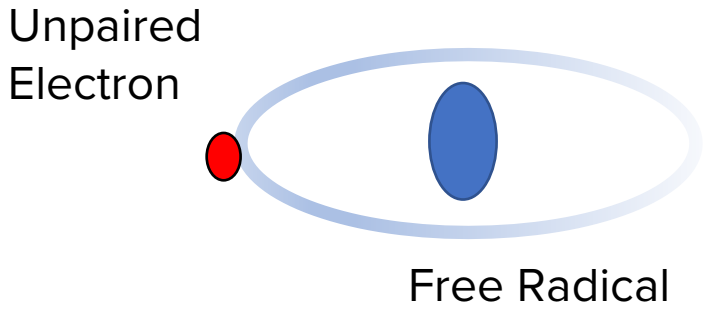
FREE RADICALS

Free Radical = any atom (or atom within a molecule) with at least one unpaired electron in its outermost shell/ orbital



Why do we want to limit their actions?

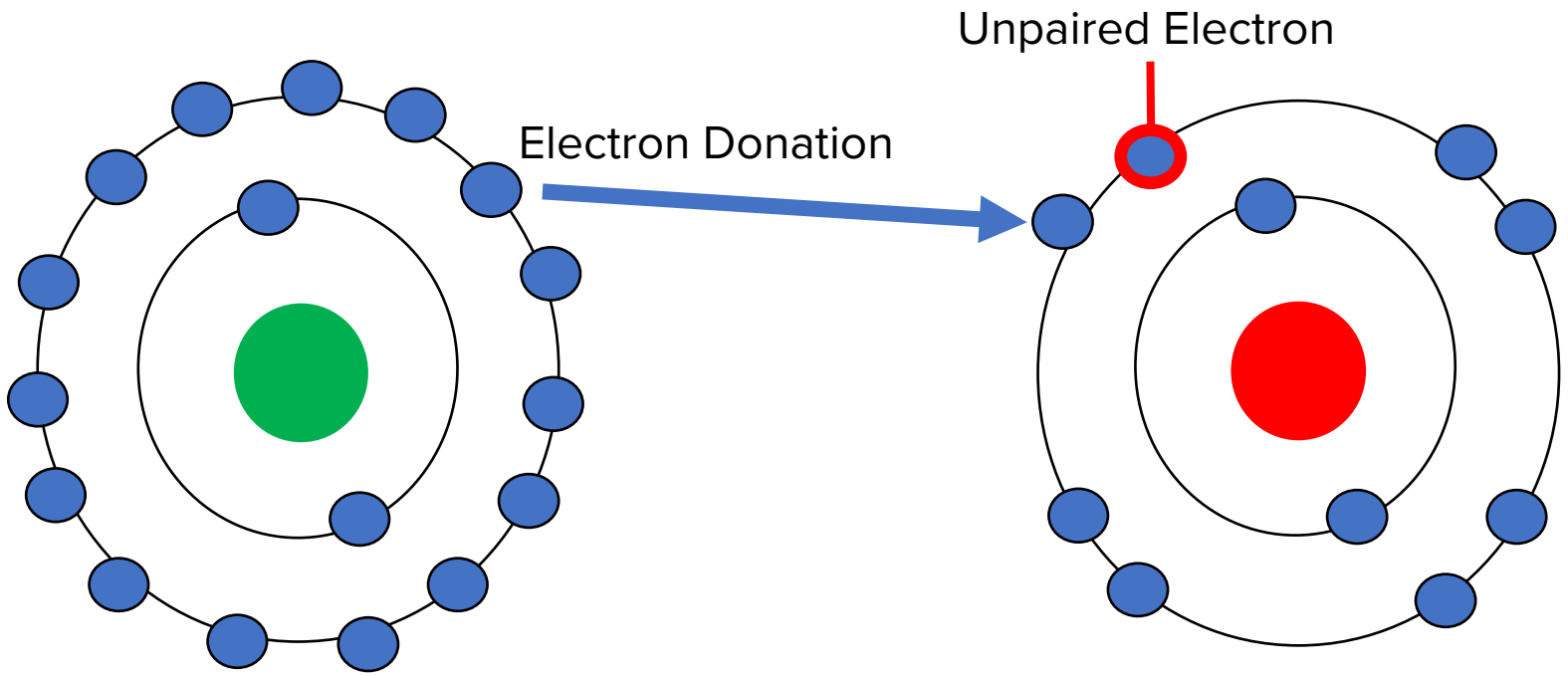
- Highly reactive
- Free radicals damage membranes (lipids), proteins, & DNA
- Can result in mutations



NOTE:
Radicals are produced as a part of normal metabolism and are necessary to life!
Excessive amounts of radicals are harmful because of their reactivity.
Also produced by processes outside of normal metabolism (e.g.-radiation, smoking, pollutants, herbicides, pesticides)

Jeukendrup & Gleeson. Champaign, IL. *Human Kinetics*. 2004
Maughan & Gleeson. *Oxford University Press*. 2010

HOW ANTIOXIDANTS REDUCE FREE RADICALS



ANTIOXIDANT

FREE RADICAL

FREE RADICALS DURING EXERCISE

Skeletal muscle continuously produces ROS and NO

- ↑ dramatically during exercise
- Repetitive contractions ↑ ROS content

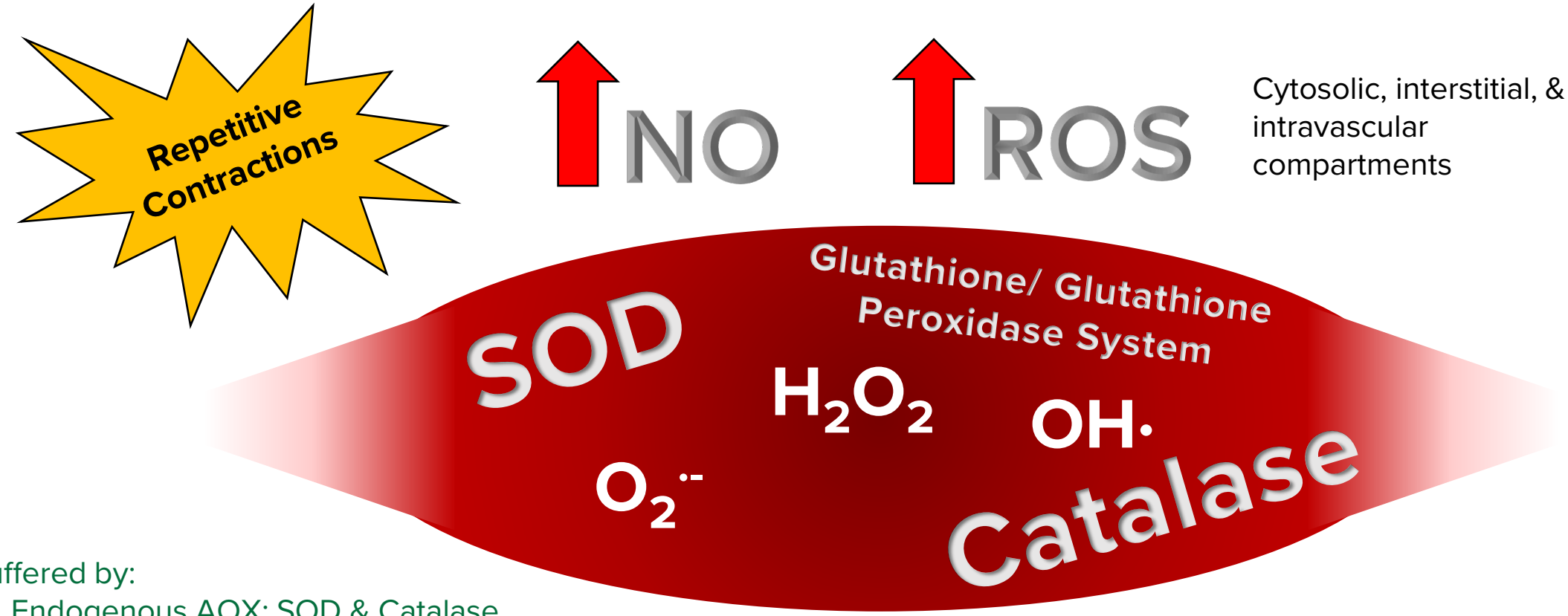
Buffered by endogenous antioxidants in the muscle:

- Superoxide Dismutase (SOD)
- Catalase

Major antioxidant pathway in the muscle:

- Glutathione/glutathione peroxidase system
  - Buffers an array of oxidant species

FREE RADICALS DURING EXERCISE



Buffered by:

- Endogenous AOX: SOD & Catalase
- Glutathione/glutathione peroxidase system

REDOX BALANCE

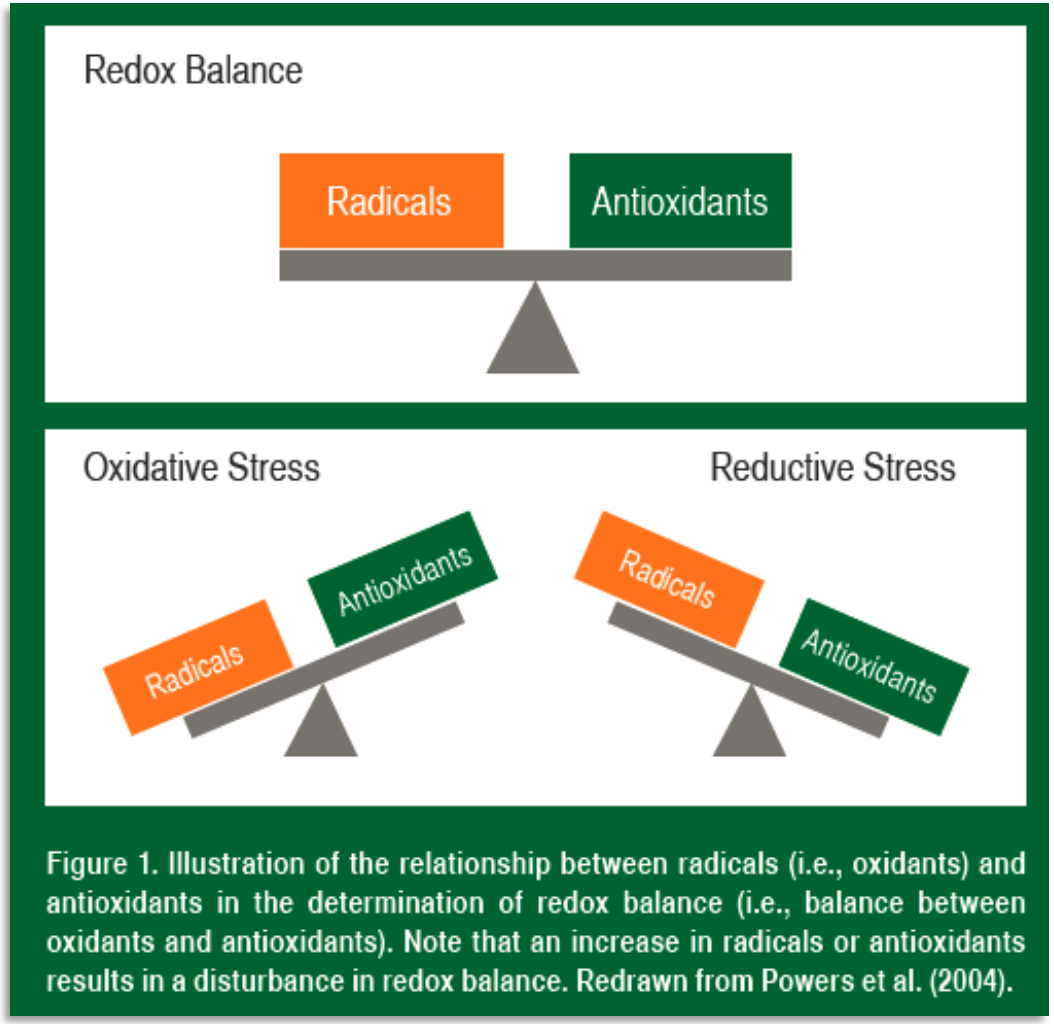


Figure 1. Illustration of the relationship between radicals (i.e., oxidants) and antioxidants in the determination of redox balance (i.e., balance between oxidants and antioxidants). Note that an increase in radicals or antioxidants results in a disturbance in redox balance. Redrawn from Powers et al. (2004).

- Exercise can alter **"redox balance"** and result in oxidative stress
  - Imbalance between radical production and muscle antioxidants
  - Muscle cells contain endogenous antioxidants to scavenge radicals

- Regular bouts of endurance exercise result in increased endogenous antioxidant enzymes in trained skeletal muscles
  - Improved ability to protect against exercise-induced oxidative stress in skeletal muscles
  - Highly trained endurance athletes have well-adapted endogenous buffer systems

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OXIDATIVE STRESS MECHANISMS

- Elevated oxidants disrupt potassium regulation
  - ⬇ Skeletal muscle Na+/K+ pump
  - ⬆ K+ concentration
- Exercise associated oxidants:
  - Limit the bioavailability of circulating NO
  - Restrict blood flow
  - Depress changes in hematological indices
- Oxidative stress:
  - Lessen endurance exercise
    - K+ regulation and perfusion
- Elevated oxidants:
  - ⬇ fat oxidation & circulating glucose while ⬆ lactate

ANTIOXIDANT MECHANISMS

Enzymatic and nonenzymatic antioxidants prevent oxidation initiated by ROS by:

- Preventing ROS formation
- Scavenging reactive metabolites and converting them to less reactive molecules
- Binding transition metal ion catalysts and preventing initiation of free radical reactions
  - E.g. copper to iron
- Preventing continued hydrogen abstraction from fatty acid chains
- Providing a favorable environment
  - Effective functioning of other antioxidants
  - Regenerating nonenzymatic antioxidant molecules

REMEMBER: *Exercise TRAINING INCREASES the levels of antioxidant enzymes

ANTIOXIDANT MECHANISMS

ROS Does Contribute to Fatigue

Despite these protective mechanisms high rates of ROS production can exceed the antioxidant capacity of myofibers, promoting oxidative stress and depressing the force of muscle contraction.

So Why Not Supplement with Antioxidants?

ANTIOXIDANTS

Antioxidants Good & Radicals Bad?

The familiar dichotomy that free radicals are bad, and antioxidants are good is pervasive in popular culture. Athletes believe that antioxidants improve performance.

Antioxidants (Good)

Antioxidants give an extra electron to the free radical.

Free Radicals (Bad)

Caused by pollution, UV radiation, x-rays, stress, strenuous exercise and other factors.

Damage Stopped

Neutralized, the chain of free radicals stops. Atom becomes stable.

https://www.drinkbai.com/whats-inside

Is it True?

ANTIOXIDANTS

Sense or Nonsense?

Should Athletes Supplement with Antioxidants?

Why might this be beneficial?
- May scavenge free radicals during activity
- May be important for those that are deficient

Why might this be detrimental?
- Not proven to improve performance
- May blunt the training response

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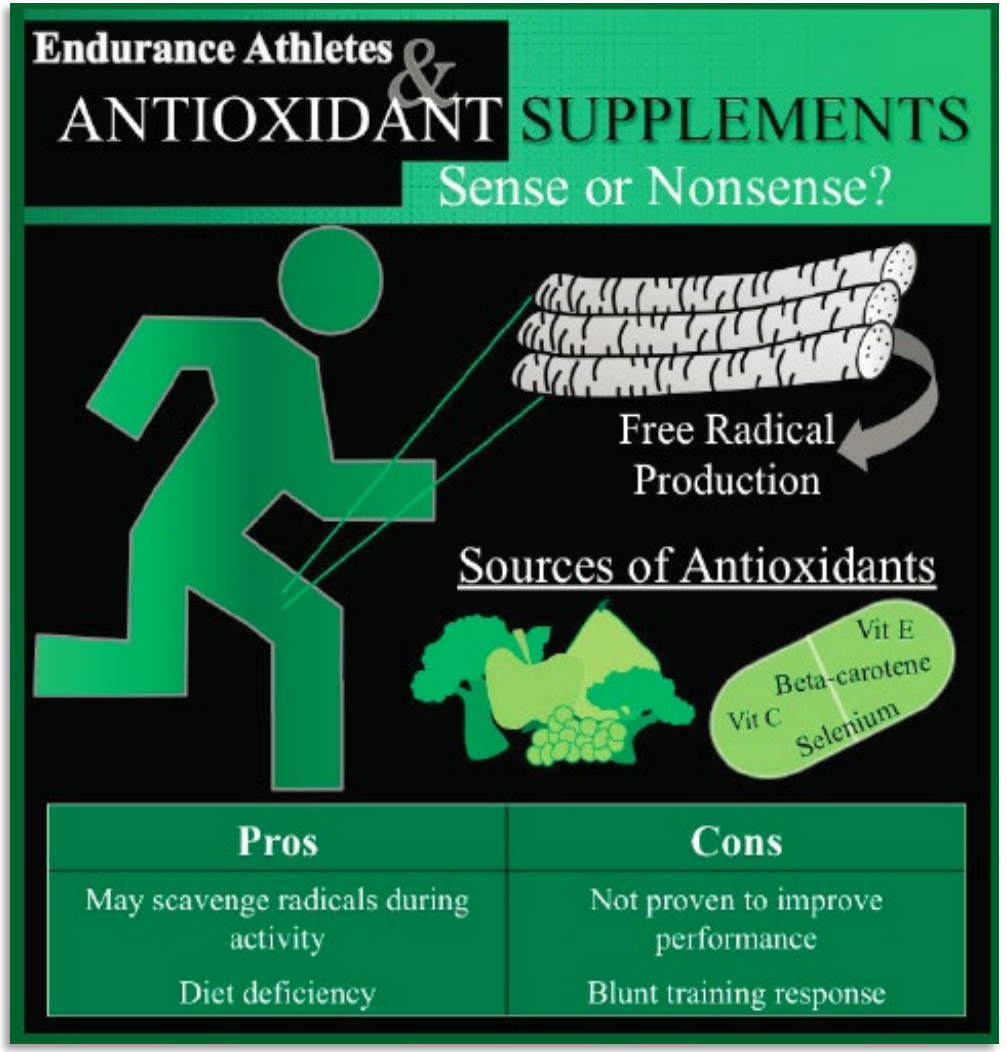


ANTIOXIDANT SUPPLEMENTATION & EXERCISE

Many antioxidants do not improve exercise performance

- Including: Vitamin C, Vitamin E, Resveratrol, Coenzyme Q10, Quercetin
- Little evidence that nutritional supplementation improves either strength or endurance exercise
- Increase antioxidant markers without ergogenic effects
- May blunt biomarkers for oxidative stress during exercise
- Exercise performance is usually unaffected, sometimes impaired

Reid M. *J Physiol*. 2016;594:5125-5133

ANTIOXIDANTS

Findings from NAC Research

The drug N- acetylcysteine (NAC) effectively opposes oxidative stress when administered systemically and is approved for use in humans (smells, mild side effects)

*First antioxidant shown to inhibit experimental muscle fatigue

- Effective at submaximal but not during near maximal contractions
  - DEMONSTRATING: Oxidants contribute to low but not high frequency fatigue
- NAC does not alter shAort term recovery of force immediately after muscle fatigue
  - DEMONSTRATING: Oxidants do not influence recovery from fatigue
- NAC increases cycling endurance
  - Time to task failure
- Delays fatigue in repeated bouts of damaging exercise

DIETARY NITRATE RESEARCH

- Can increase exercise efficiency and improve performance
- Mechanisms include:
  - Greater ATP supply via altered mitochondrial respiration
  - More efficient ATP utilization during muscle contraction
- Increase bioavailability of NO derivatives
  - Promotes NO signaling
- Buccal flora convert nitrate to nitrite
  - Via bacterial nitrate reductase
- Circulating Nitrite is converted to NO
- Central nervous system
  - Modulation of cortical function

Reid M. *J Physiol*. 2016;594:5125-5133

Take Homes: NAC & NO

Thiol antioxidants (like NAC) and dietary nitrates appear to improve endurance exercise

- Safe for human use
  - Laboratory doses
  - Both effective as a single dose shortly before exercise
  - Both work via redox mechanisms
- Thiols are not practical for widespread use
- Thiols preserve contractile function of myofibers
  - Buffer exercise induced ROS
- Dietary nitrates increase exercise efficiency
  - Augment NO actions on mitochondrial metabolism, blood flow distribution, or both

RISKS OF HIGH DOSE SUPPLEMENTATION

- ROS are important intermediate messengers in apoptosis pathways
  - Antioxidants may inhibit apoptosis
    - Necessary defense mechanism to inhibit tumor development/ mutated cells
- Prevents effective removal of damaged cells
- Side effects of excessive vitamin intake
- Can impair athlete's exercise induced training adaptations

RISKS OF HIGH DOSE SUPPLEMENTATION

Muscle recovery from damaging exercise is mediated in part by oxidant signaling

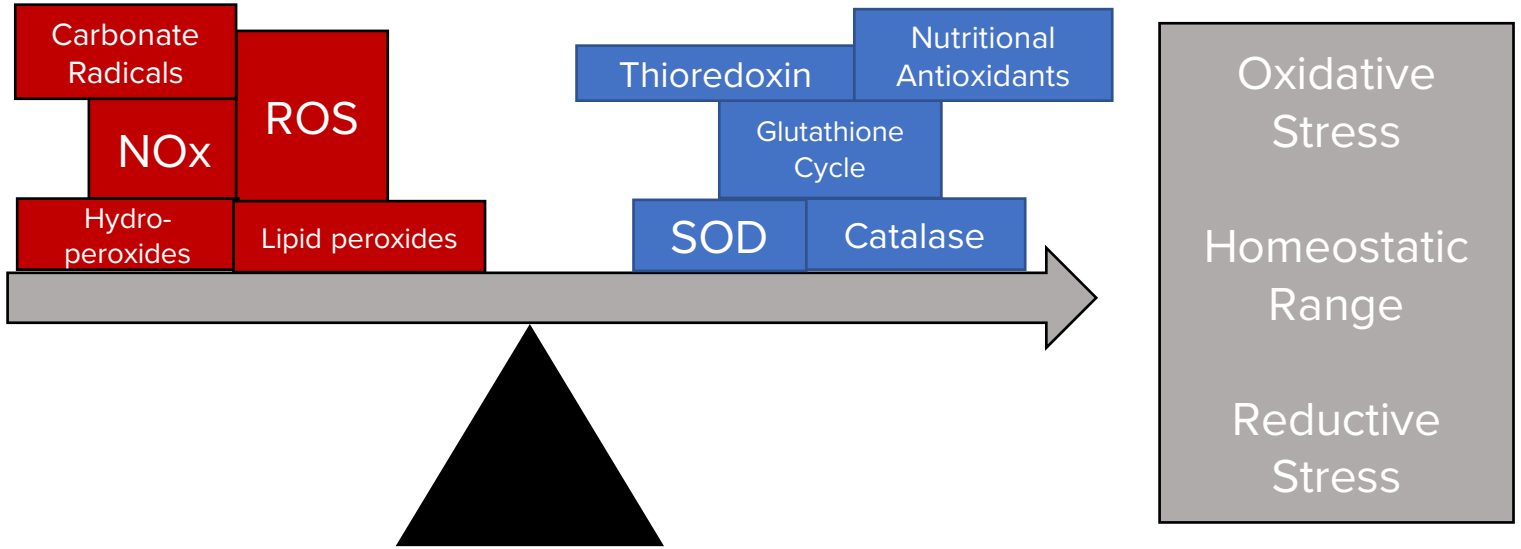
- Antioxidants can blunt:
  - Signaling events
  - Repair mechanisms
- Training responses to exercise can be depressed
  - ⬇ mitochondrial biogenesis
  - ⬇ insulin sensitivity
- One dose can:
  - ⬇ exercise induced vasodilation
  - Inhibit post exercise increases in HSPs

Reid M. *J Physiol*. 2016;594:5125-5133

BALANCE

It's a Balance!

ROS are necessary! ROS play an important role in the regulation of signaling pathways that are required to promote skeletal muscle adaptation in response to both exercise and physical activity.



ROS: A NEW VIEW

OLD VIEW: ROS are by-products of metabolism and have only deleterious effects on muscle function.

NEW VIEW: Specific ROS are generated in a controlled manner by skeletal muscle fibers in response to physiological stimuli and play important roles in the physiological adaptations of muscle to contractions that result in muscle adaptation.

MICRONUTRIENTS AS ANTIOXIDANTS

Vitamins that act as antioxidants include:

Vitamin A

Vitamin C

Vitamin E

Beta carotene

Vitamin E:

- Free radical scavenger
- Prevents initiation and propagation of lipid peroxidation in cellular membranes
- Maintains membrane stability

Vitamin C:

- Capable of regenerating vitamin E in the antioxidant cascade

MICRONUTRIENTS AS ANTIOXIDANTS

Minerals

Several minerals are components of antioxidant enzymes involved in the defense of free radicals:

- Selenium
  - Cofactor of glutathione peroxidase
  - Influences quenching of ROS
- Copper
- Manganese

POLYPHENOLS

POLYPHENOLS

A compound containing more than one phenolic hydroxyl group

Scavenge peroxyl, superoxide, and NO radicals

Flavonoids are a subclass of polyphenols that include:

- Flavanols, flavanones, and anthocyanidins
- Contain phenolic hydroxyl groups attached to their ring structures that give antioxidant activity

Name foods that contain polyphenols.

POLYPHENOL INTAKE

- Can be classified into flavonoids and non-flavonoids
- Food sources rich in polyphenols include:
  - Onions
  - Apples
  - Tea
  - Red wine
  - Red grapes
  - Strawberries
  - Raspberries
  - Blueberries
  - Cranberries
  - Certain nuts
- Average polyphenol intake is relatively undetermined
  - Dutch estimated to eat 23 mg/day of flavones and flavanols
  - Small amount may have significant effects

POLYPHENOLS

Nonflavonoids	Sources
Ellagic acid	Strawberries, blueberries, raspberries
Coumarins	Bell peppers, bok choy, cereal grains, broccoli

Flavonoids	Sources
Anthocyanins	Red fruits
Catechins	Tea, wine
Flavanones	Citrus
Flavones	Fruits and vegetables
Flavanols	Fruits, vegetables, tea, wine
Isoflavones	Soybeans

POLYPHENOL PROTECTION?

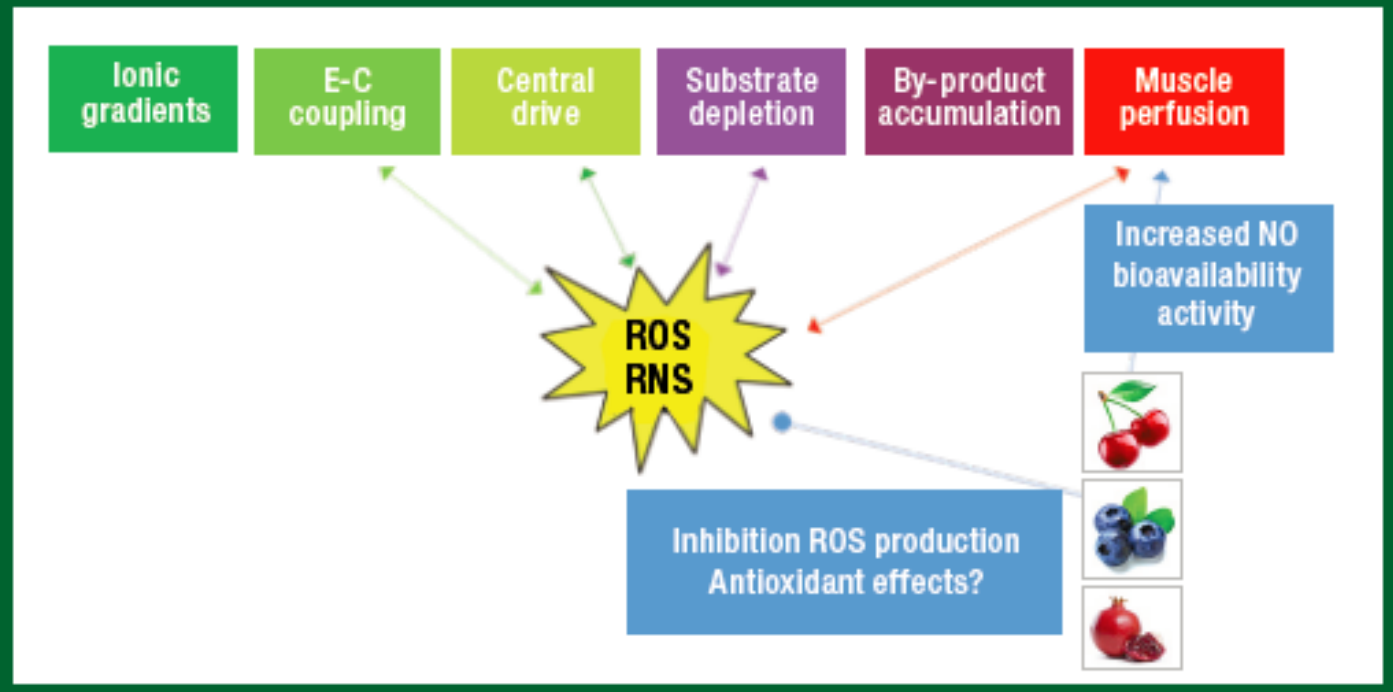


Figure 1. The potential mechanisms of exercise-induced fatigue. The mechanisms of fatigue remain controversial due to its complex multifactorial nature and specificity to exercise mode, intensity and duration. However, increased reactive oxygen and nitrogen species exposure during exercise has been implicated, suggesting that polyphenol supplementation may prove ergogenic due to their antioxidant properties.

≈500 mg/day of total flavonoids or 300 mg/day procyanidins

- Unlikely that plasma phenolics are direct antioxidants *in vivo*
- May increase endogenous antioxidant capacity
- *In vitro* anti-inflammatory properties
- Improvement in flow mediated dilation

SSE#195

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Bowtell et al, Sports Science Exchange (2019) Vol. 29, No. 195, 1-5

POLYPHENOL SUPPLEMENTATION?

Preliminary studies suggest:

- ≈300 mg of polyphenol 1 h prior to exercise
  - Recreationally active
  - Enhance endurance performance
  - Enhance repeated sprint performance
  - Mediated via vascular mechanisms
- Recovery of muscle strength and performance may be enhanced
  - Optimal dose & blend unknown
  - Suggested consumption:
    - ≈1200 mg/d Montmorency cherry or pomegranate polyphenols for >3 days prior to exercise

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POLYPHENOL SUPPLEMENTATION?

"Evidence is insufficient to make recommendations for or against the use of polyphenol supplementation (neither specific polyphenols nor specific doses) for either recreational, competitive or elite athletes."

Myburgh KH. *Sports Med*. 2014;*44(1):57-70*

KEY TAKEAWAYS

Antioxidants:

- ✓ Antioxidants limit the action of free radicals
- ✓ Exercise training improves antioxidant capacity
- ✓ Little to no evidence for supplementation, consume in diet
- ✓ ROS play an important role in adaptation to exercise

Polyphenols:

- ✓ Scavenge radicals
- ✓ May provide protection through multiple mechanisms
- ✓ More research is needed

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