Nrf2 Pathway and the Reduction of Oxidative Stress

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Oxidative stress has been linked to cellular damage initiating disease processes such as cardiovascular disease, diabetes, and cancer. The Nuclear factor erythroid derived 2 (Nrf2) pathway (Figure 1) is an age-related cellular defense. The purpose of this study was to define the relationship between Protandim, an activator of the Nrf2 pathway, and cellular oxidative stress in healthy and cancerous cells to determine if Protandim could activate the Nrf2 pathway and induce antioxidant enzymes, thereby protecting cardiomyocytes from apoptosis. Results indicated that treated cardiomyocytes showed increased levels of Nrf2 nuclear accumulation, activation of endogenous antioxidant enzymes, and protection against cell induced oxidative stress (p<0.001). Quereshi et al. (2010) completed a study to delineate if Protandim decreased oxidative stress through the Nrf2 pathway. After six months of supplementation, TRAMs decreased by 46% (p<0.001), and plasma TBARS decreased by 57% (p<0.01). In 2005, Nelson et al. conducted a study to determine if Protandim decreased cellular damage. After 30 days of supplementation, TRAMs decreased by 46% (p<0.001), and superoxide dismutase and catalase increased by 50% and 54% respectively. The results from studies indicate that Protandim’s activation of the Nrf2 pathway increased endogenous antioxidant availability, resulting in decreased oxidative stress and age-related cellular damage.

**LITERATURE REVIEW**

**Keap1-Nrf2 Pathway**

Under normal conditions, Nrf2 is ubiquitinated through Keap1 and degraded. Exposure to oxidative stress causes inactivation of Keap1. Nrf2 accumulates in the nucleus and activates multiple cytoprotective genes (Muniswamy, Y., Moistakis, H., & Yamamoto, M. (2012)).

- Nelson et al. (2005) found that Protandim decreased cellular damage. After 30 days of supplementation, TRAMS decreased 46% (p<0.001), and superoxide dismutase and catalase increased by 50% and 54% respectively (Figure 3).
- In 2005, Nelson et al. conducted a study to determine if Protandim decreased cellular damage. After 30 days of supplementation, TRAMS decreased by 46% (p<0.001), and superoxide dismutase and catalase increased by 50% and 54% respectively. The results from studies indicate that Protandim’s activation of the Nrf2 pathway increased endogenous antioxidant availability, resulting in decreased oxidative stress and age-related cellular damage.

**RESULTS**

In adult patients, does a diet containing the supplement Protandim compared to a diet not containing the supplement Protandim, lower overall cellular oxidative stress?

### RESEARCH QUESTION

In adult patients, does a diet containing the supplement Protandim compared to a diet not containing the supplement Protandim, lower overall cellular oxidative stress?

### DISCUSSION

**Plasma TRAMs: Protandim vs. Control Group**

- Nelson et al. (2005), Quereshi et al. (2010), Burman et al. (2012), and Reuland et al. (2013) conducted studies that resulted in decreased TRAMs.
- Liu et al. (2009), Donovan et al. (2012), and Reuland et al. (2013) conducted studies that resulted in increased levels of antioxidants.
- Robbins et al. (2010), and Reuland et al. (2013) conducted studies that resulted in decreased levels of cellular oxidative stress.
- Nelson et al. (2005), Li et al. (2009), Quereshi et al. (2010), Robbins et al. (2010), Burman et al. (2010), Donovan et al. (2012), and Reuland et al. (2013) conducted studies that resulted in decreased levels of cellular oxidative stress.

### Figure 2. Plasma TRAMs: Protandim vs. Control Group

- Plasma TRAMs decreased by 60% in Protandim group (p=0.001) versus 48% in control group (p=0.01) (Quereshi et al. 2010).
- Nelson et al. (2005), Quereshi et al. (2010), Burman et al. (2012), and Reuland et al. (2013) conducted studies that resulted in decreased TRAMs.
- Liu et al. (2009), Donovan et al. (2012), and Reuland et al. (2013) conducted studies that resulted in increased levels of antioxidants.
- Robbins et al. (2010), and Reuland et al. (2013) conducted studies that resulted in decreased levels of cellular oxidative stress.
- Nelson et al. (2005), Li et al. (2009), Quereshi et al. (2010), Robbins et al. (2010), Burman et al. (2010), Donovan et al. (2012), and Reuland et al. (2013) conducted studies that resulted in decreased levels of cellular oxidative stress.

### APPLICATION TO CLINICAL PRACTICE

**Applicability to Clinical Practice**

- Cellular insult from reactive oxygen species is unavoidable. They are responsible for damage to cell membranes, DNA, and tissues. This damage can lead to premature aging and initiation of disease processes such as cancer, heart disease, neurodegenerative diseases, and macular degeneration.
- Endogenous antioxidants are modulated through the Nrf2 pathway. NRF2 also plays a role in cancer development and suppression through antioxidant enzymes.
- Scientific evidence has shown that Protandim induces the Nrf2 pathway, increases endogenous antioxidant production and provides cellular protection from damage due to oxidative stress.

### Oxidative Stress and Disease

Oxidative stress is a state in which free radicals overwhelm the body’s antioxidant defense mechanisms. This process has been implicated in the development of many diseases (Nunes, 2010).