

# Analgesic and anti-inflammatory properties of a phycocyanin-enriched microalgae extract CyaninPlus™.

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## Objective and methodology

The objective for this research was to document the anti-inflammatory properties of the microalgae extract in vitro and in vivo.

A panel of in vitro tests addressed the following:

- Antioxidant capacity
- Inhibition of inflammatory enzymes COX-2 and Lipoxygenase
- Reduction of free radical production by inflammatory cells

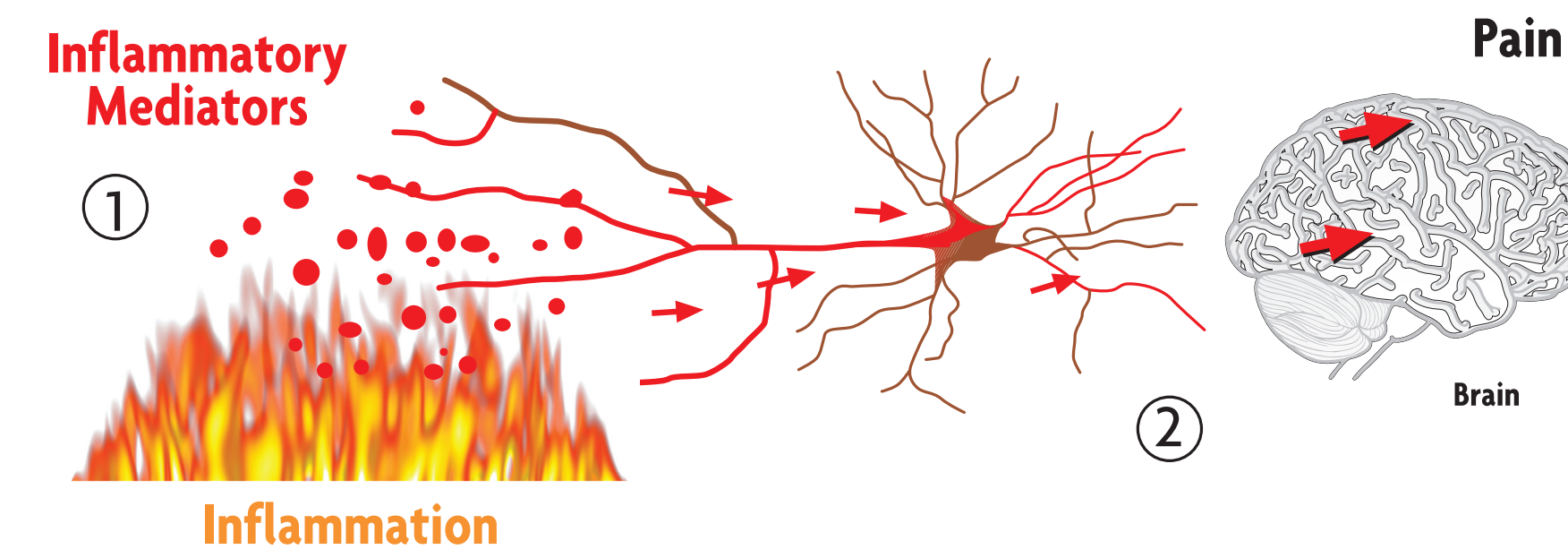
Two human clinical pilot studies were performed:

- An open-label 4-week study on 12 people 40-70 years of age suffering from chronic joint pain
- A double-blinded placebo-controlled cross-over study involving 12 people in the same age range, where each consumption phase was 1 week, separated by a wash-out period of one week.

## Background

Inflammation is an integral part of normal processes such as the acute response to bacterial infection. However, in the chronic state, inflammation contributes to a wide range of conditions of failing health, including chronic pain, joint problems, cardiovascular disease, arthritis, obesity, cognitive decline, mood disorders and depression.

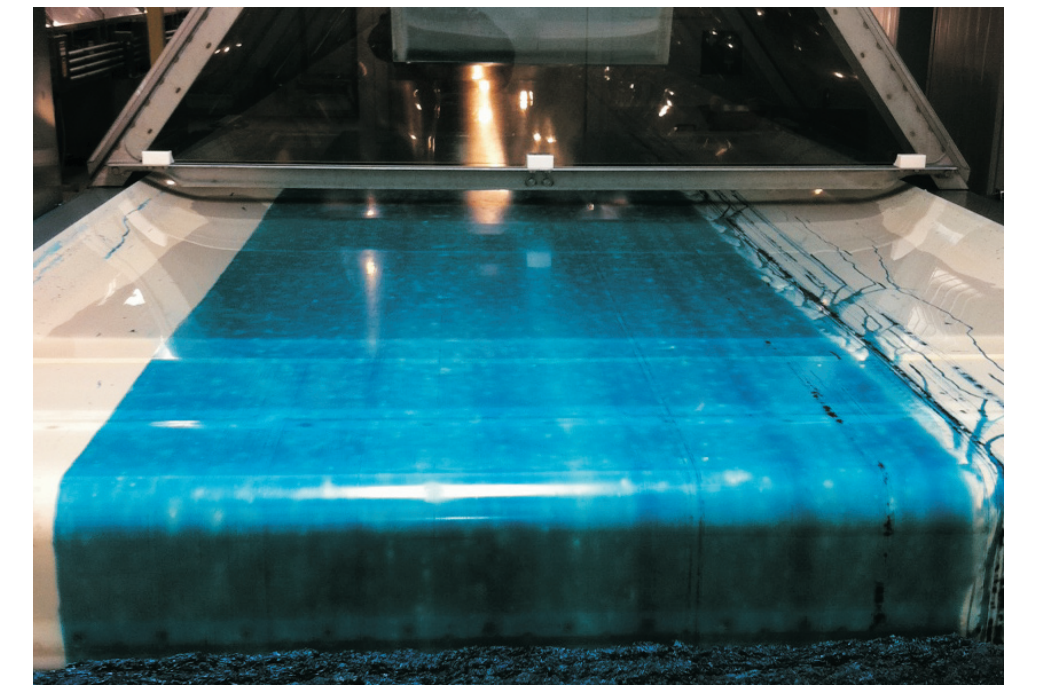
Natural products that help reduce inflammation are currently receiving serious attention as natural, food-based support of functionality and alternatives to over-the-counter products such as NSAIDs. The microalgae extract CyaninPlus™ is a food product that recently received self-affirmed GRAS status. It is enriched with Phycocyanin, and standardized based on Phycocyanin content. In addition, it contains another natural fraction of the microalgae, shown to possess additional and complementary anti-inflammatory properties.



## Bioactive compounds in CyaninPlus™.

CyaninPlus™ is a proprietary cyanophyta extract derived from *Arthrospira* (ssp. *platensis* or *maxima*). CyaninPlus™ is produced by aqueous extraction and dried using the proprietary HydroDri™ technology.

The primary component of CyaninPlus™ is Phycocyanin, which is known to act as an antioxidant and a selective COX-2 inhibitor [1] with documented anti-inflammatory properties [2-9]. In addition to Phycocyanin, CyaninPlus™ contains anti-inflammatory compounds different from Phycocyanin yet with complementary anti-inflammatory properties. CyaninPlus™ is a natural extract that promotes anti-inflammatory and pain-relieving activity.



Bioactive compounds	Health/Nutrition outcomes
Phycocyanin	Anti-inflammatory, antioxidant, COX-2 inhibition
Non-Phycocyanin antioxidant compounds	Reduction of oxidative stress, cellular protection
Non-Phycocyanin anti-inflammatory compounds	Anti-inflammatory, Lipoxygenase inhibition
Immune modulating compounds	Support of anti-viral defense mechanisms

## In vitro data

Figure 1. The antioxidant capacity of CyaninPlus™ was tested in the Folin-Ciocalteu assay, the total antioxidant capacity assay, and the CAP-e cellular antioxidant protection assay. The antioxidant capacity of CyaninPlus™ was demonstrated in all three assays. The antioxidant capacity of CyaninPlus™ was not only due to the content of Phycocyanin (PC), since the non-PC fraction showed even higher antioxidant capacity per gram. This suggests that antioxidant compounds other than PC contribute to the total antioxidant capacity of CyaninPlus™.

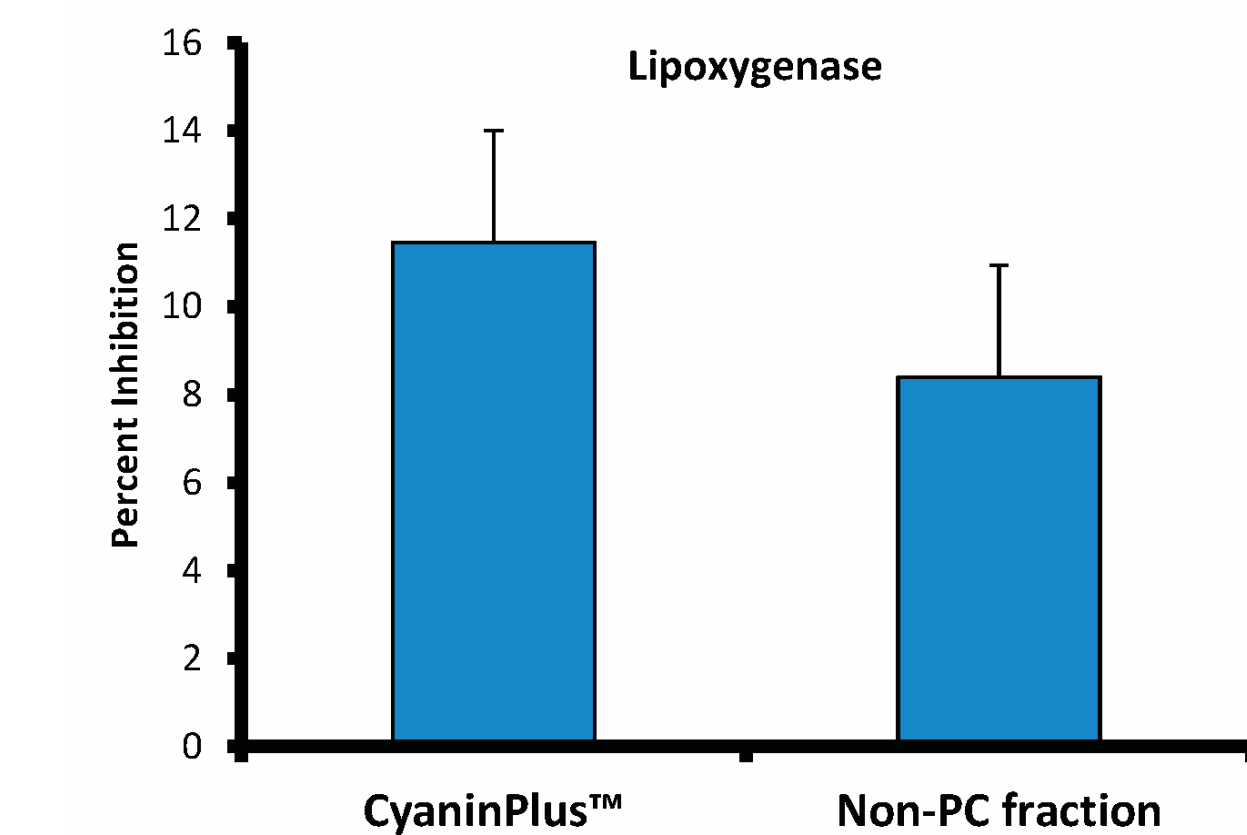
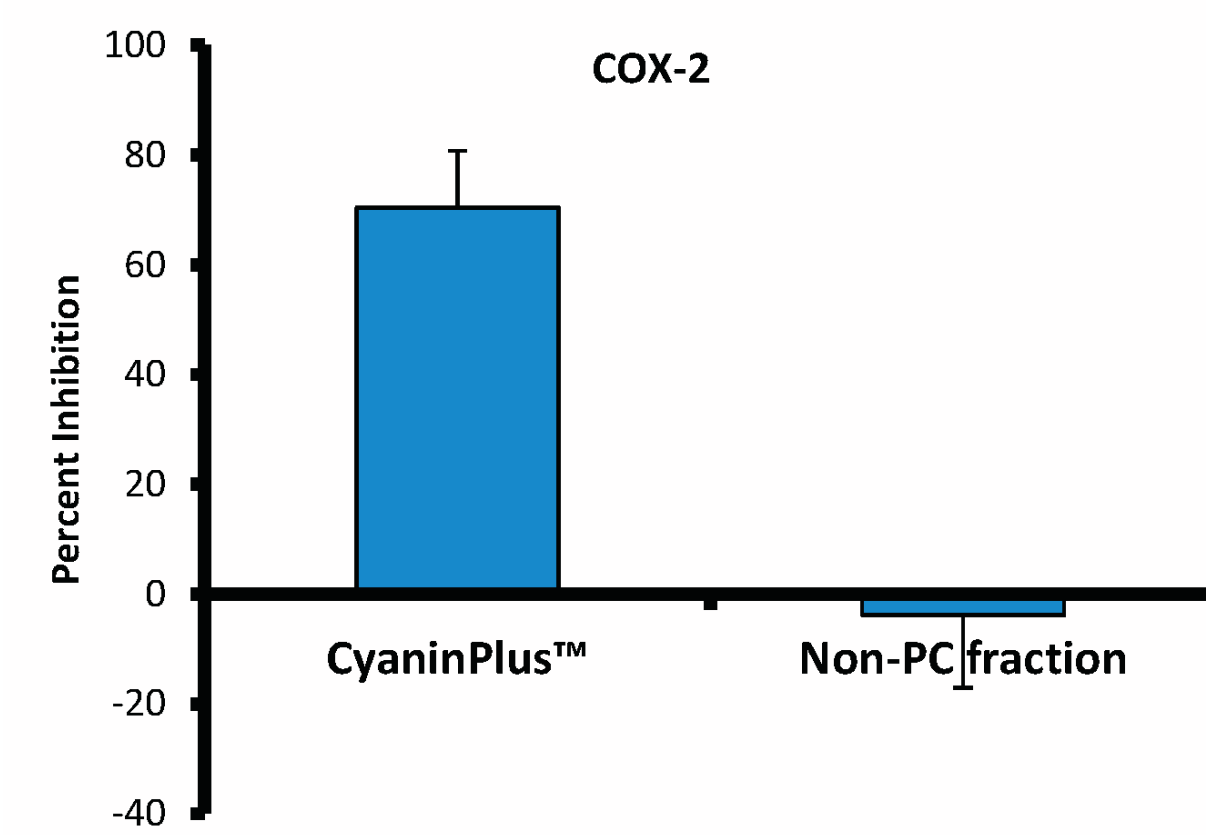
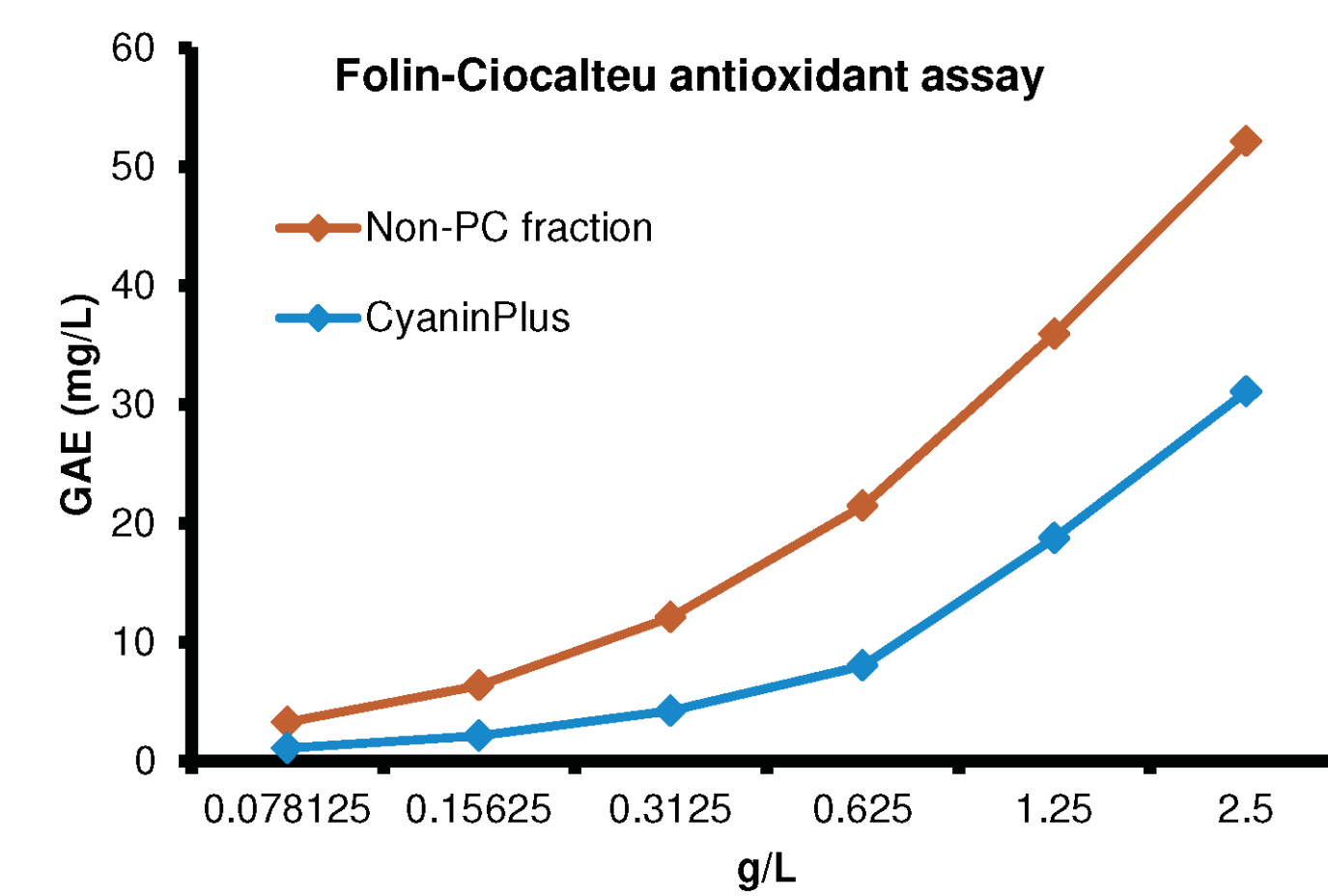


Figure 2. CyaninPlus™ has several synergistic mechanisms of action pertaining to anti-inflammatory properties: 1) Phycocyanin is responsible for the COX-2 inhibiting property of CyaninPlus™; 2) Compounds other than Phycocyanin ("Non-PC Fraction") inhibit inflammatory actions by a different pathway, namely by inhibition of the enzyme Lipoxygenase. The bimodal action may be one of the underlying mechanisms for the analgesic effects of CyaninPlus™.

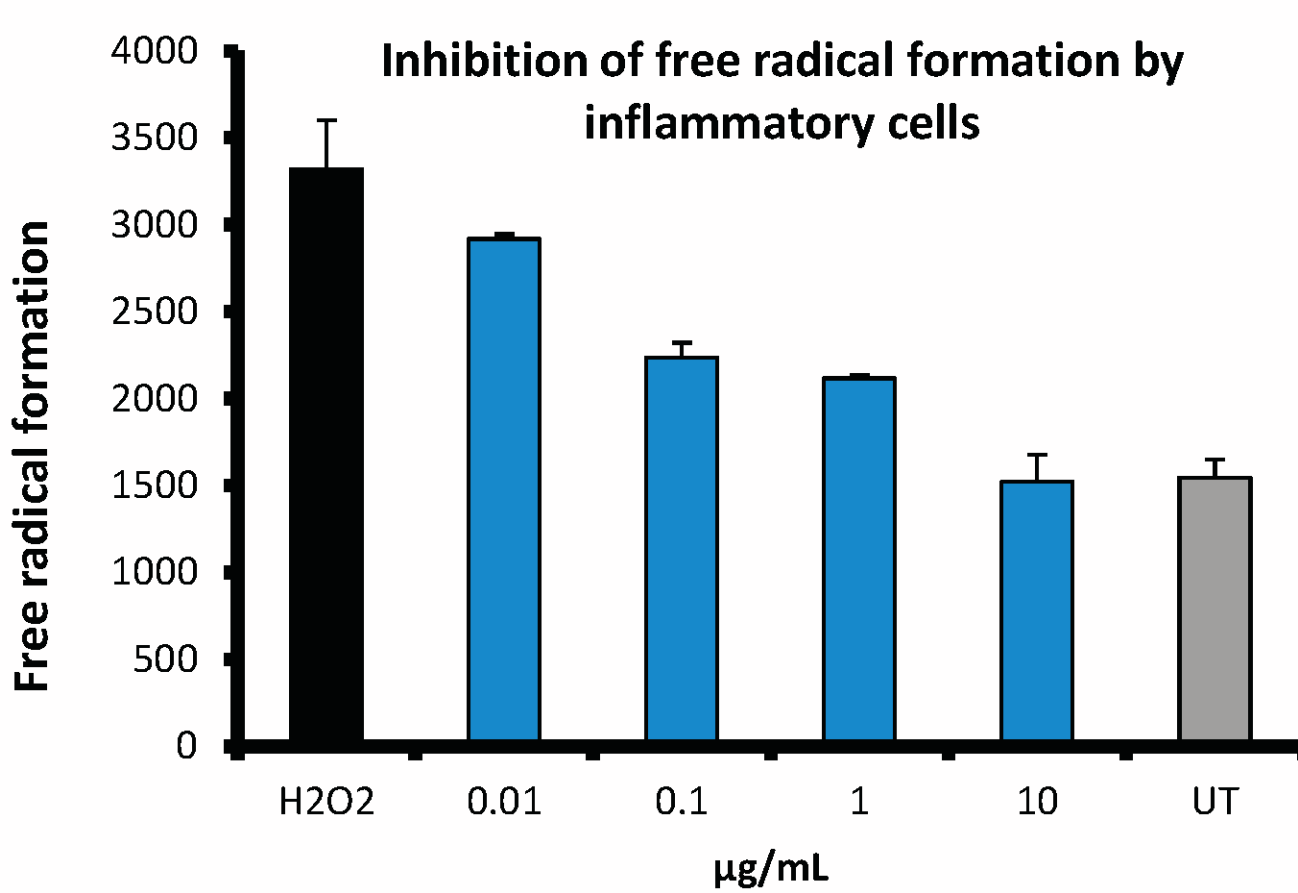


Figure 3. CyaninPlus™ treatment of inflammatory cells resulted in reduced free radical formation by these cells. As a cellular model, peripheral blood polymorphonuclear cells from healthy donors were used to test this effect. Hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) was used to trigger Reactive Oxygen Species (ROS) production by the cells. A clear dose-dependent inhibition of formation of ROS was seen when the cells were treated with CyaninPlus™ before triggering ROS formation. ROS formation was completely inhibited at the highest dose of CyaninPlus™, as the free radical formation of the cells treated with 10µg/mL CyaninPlus™ produced less ROS than untreated (UT) cells. The inhibition was statistically significant at all doses tested when compared to the cells treated with H<sub>2</sub>O<sub>2</sub> only (p<0.05).

## Human clinical data

For both studies, each person's primary and secondary pain-related complaints were identified at study start. Visual analog scales (VAS) were used to track: Changes in pain for primary pain area at rest, changes in pain for primary pain area during physical activity, changes in pain for secondary pain area at rest, and changes in pain for secondary pain area during physical activity. In addition, the degree with which people were able to complete normal activities of daily living was scored. The data from the pain scores showed that reduced pain was experienced for both areas of primary and secondary pain. The improvements were seen both at rest and during physical activity.

### Open-label study

The initial open-label clinical study on CyaninPlus™ was of 4 weeks duration and involved a broad range of chronic pain complaints.

Study design: An open-label study design was used. Twelve healthy human subjects were provided with CyaninPlus™ for 4 weeks, with weekly follow-up visits. At baseline and at 1, 2, 3, and 4 weeks of consumption, study participants were interviewed and data pertaining to pain and activities of daily living were collected using Visual Analog Scales.

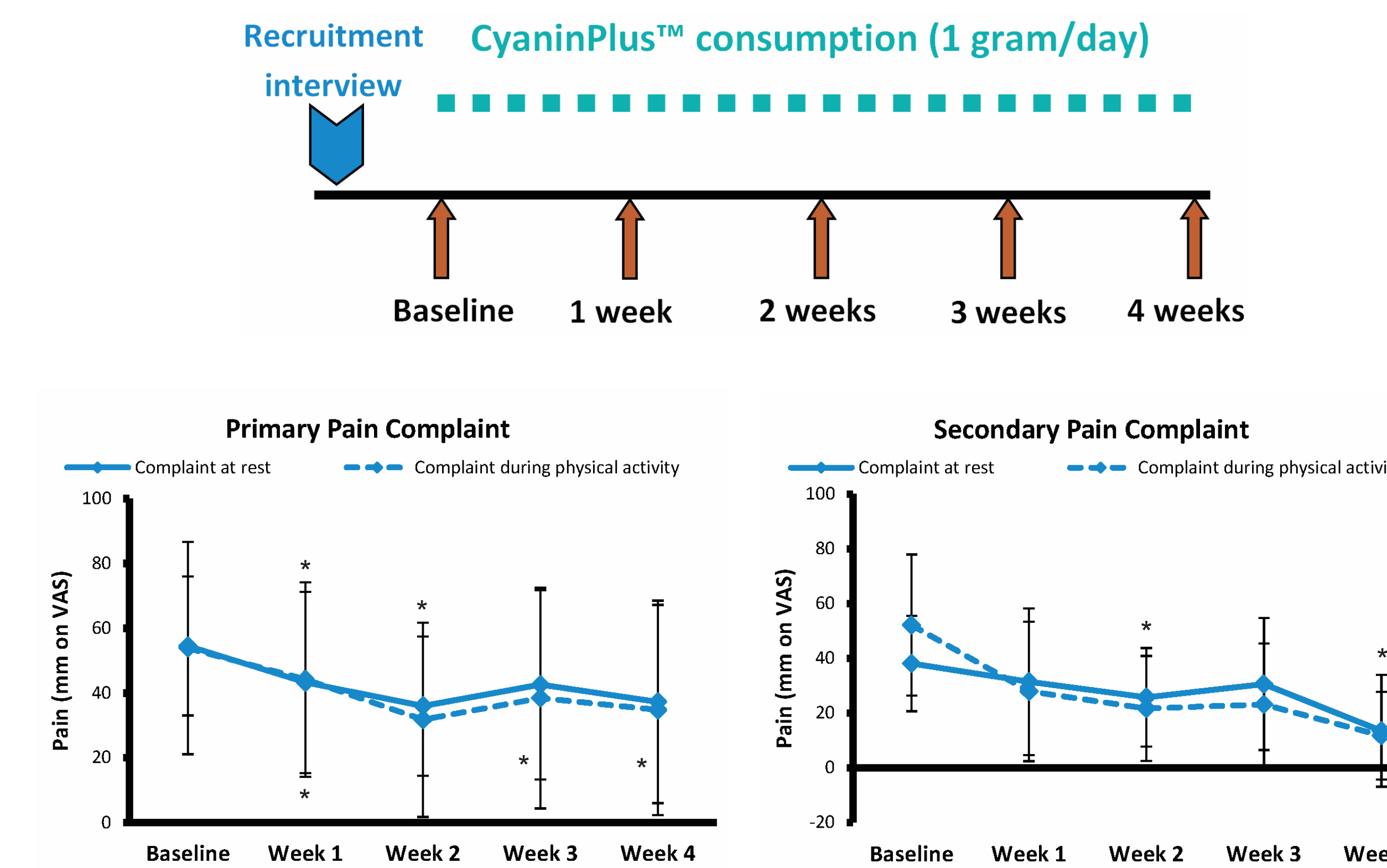


Figure 4. CyaninPlus™ consumption (1 gram daily) provided relief of primary and secondary pain-related complaints, both at rest (solid lines) and during physical activity (dashed lines). Asterisks show data points where statistically significant pain reduction from baseline was seen (p<0.05), using within-subject analysis.

### Placebo-controlled dose study

A subsequent placebo-controlled cross-over dose study was performed.

Study design: A single-blinded placebo-controlled cross-over study design was used. Twelve healthy human subjects were provided with CyaninPlus™ or placebo, according to the schedule shown in the diagram below. At baseline and at 1, 2, 3, 4 and 5 weeks of consumption, study participants were interviewed and data pertaining to pain and activities of daily living were collected using Visual Analog Scales.

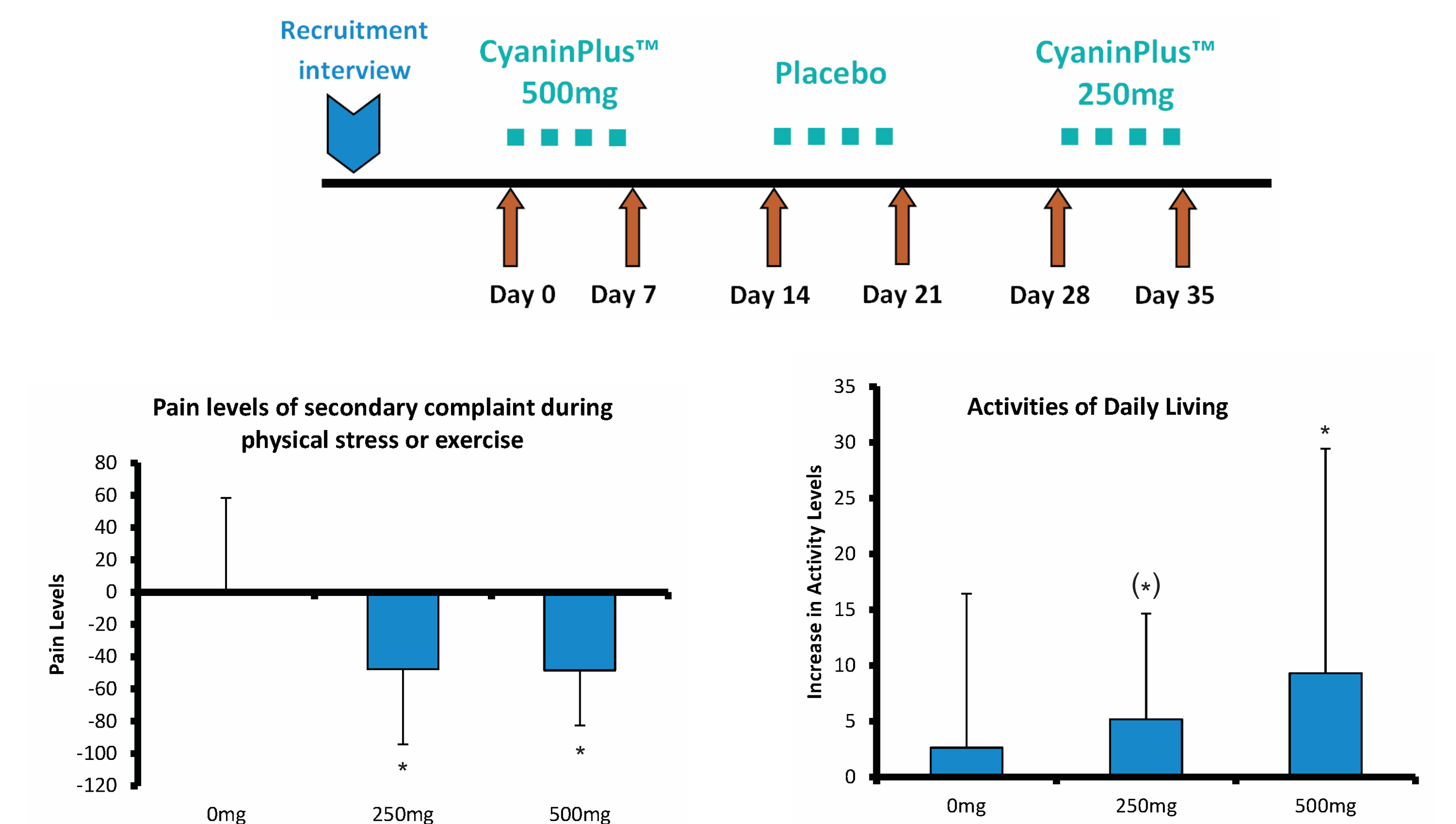
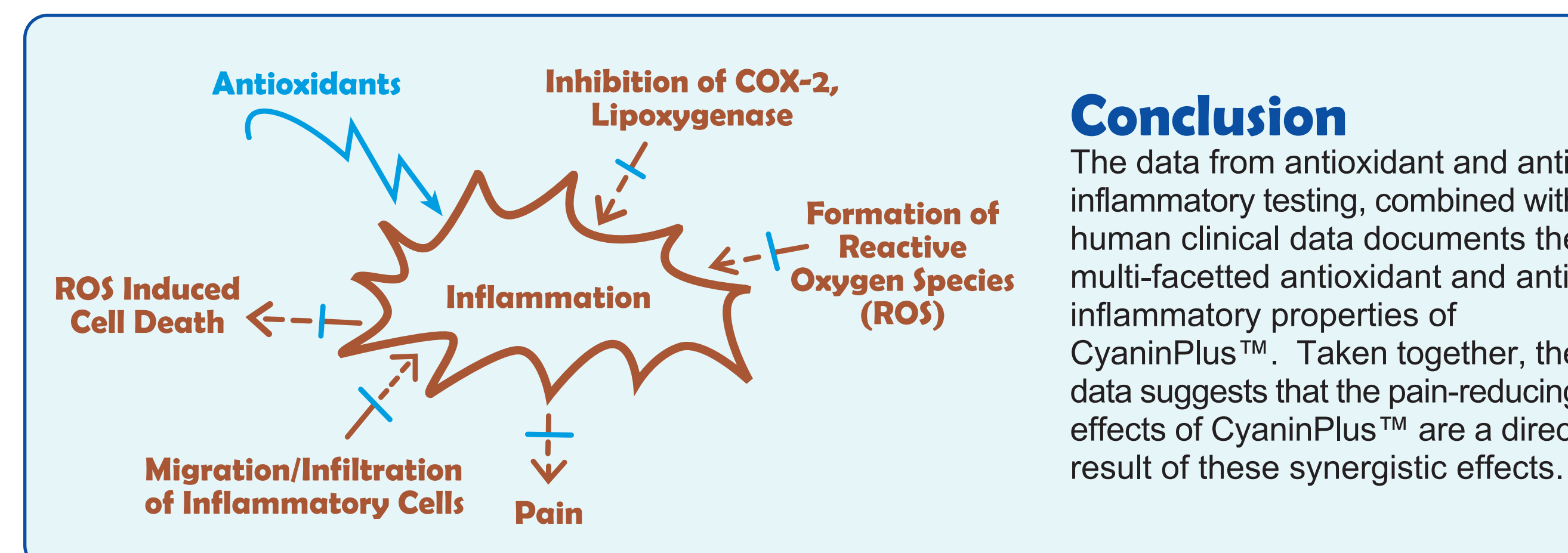


Figure 5. CyaninPlus™ (250mg, 500mg daily) or placebo (0mg daily) consumption for 7 days, separated by 7-day washout periods, showed reduction in minor pain complaints and increased ability to perform activities of daily living. Asterisks show data points where statistically significant pain reduction from baseline was seen (p<0.05), using within-subject analysis.



## Conclusion

The data from antioxidant and anti-inflammatory testing, combined with human clinical data documents the multi-faceted antioxidant and anti-inflammatory properties of CyaninPlus™. Taken together, the data suggests that the pain-reducing effects of CyaninPlus™ are a direct result of these synergistic effects.

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## References

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