ORIGINAL RESEARCH

Comparative Study of Synthetic vs. Natural Antioxidants in Inflammatory Diseases

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ABSTRACT

Objective: To evaluate the antioxidant capacity, anti-inflammatory effects, and potential side effects of synthetic and natural antioxidants in controlling oxidative stress in inflammatory conditions. **Methodology:** This study aimed to compare the efficacy of synthetic and natural antioxidants in reducing oxidative stress and inflammation in 100 individuals with inflammatory diseases. A randomized controlled trial was conducted with participants assigned to either a synthetic antioxidant group or a natural antioxidant group, with assessments at baseline, 3 months, and 6 months. Key outcomes measured included reactive oxygen species (ROS), inflammatory markers (C-reactive protein [CRP] and tumor necrosis factor-alpha [TNF-α]), and Disease Activity Score (DAS28). Statistical analyses, including t-tests, ANOVA, and multivariate regression, were employed to compare the changes in these markers between the two groups over time. **Result:** The results revealed that both antioxidant groups experienced significant reductions in ROS, CRP, and TNF-α, with the natural antioxidant group showing a more pronounced improvement. At 6 months, the natural antioxidant group exhibited a 53.5% reduction in ROS levels, compared to a 40% reduction in the synthetic antioxidant group. Similarly, the natural antioxidant group showed greater reductions in CRP and TNF-α, and a significantly lower DAS28 score (2.7) compared to the synthetic antioxidant group (3.5). Statistical significance was observed at both the 3-month ($p = 0.04$) and 6-month ($p = 0.02$) time points for disease activity. **Conclusion:** Natural antioxidants demonstrated superior efficacy in reducing oxidative stress, inflammation, and disease activity compared to synthetic antioxidants. These findings suggest that natural antioxidants may offer a more effective and comprehensive therapeutic approach for managing inflammatory diseases, potentially leading to better long-term clinical outcomes. Further research is warranted to explore the underlying mechanisms and the broader applicability of natural antioxidants in clinical practice.

Keywords: Oxidative stress, Inflammation, Natural antioxidants, Synthetic antioxidants, Disease Activity Score (DAS28)

BACKGROUND

Inflammatory diseases, such as rheumatoid arthritis, cardiovascular disease, and neurological ailments, have their roots in complex molecular pathways that involve oxidative stress. Many pathways are responsible for the development of many diseases characterized by inflammation. Oxidative stress can occur when the production of reactive oxygen species (ROS) is greater than the ability of the body to eliminate them via the use of antioxidants. Oxidative stress may occur when the generation of reactive oxygen species (ROS) exceeds the body's capacity to remove them via antioxidants. It is possible for reactive oxygen species, often known as ROS, to cause damage to DNA, proteins, and lipids, which may then lead to the activation of many inflammatory pathways(1).

Free radicals can cause oxidative damage to cells, which may be avoided or slowed down by molecules known as antioxidants. Free radicals can also cause harm to cells. Either by strengthening the body's natural antioxidant activities or neutralizing reactive oxygen species (ROS), they can achieve their goals. People can manufacture antioxidants in addition to the fact that biological processes produce them(2). The term "natural antioxidants" refers to naturally occurring chemicals that possess antioxidant properties derived from the natural world, whether from plants, animals, or bacteria. The term "natural antioxidant" is applicable in the context of these compounds. Incorporating natural antioxidants into one's diet regularly is a technique that has gained much popularity. Included in this category are items like enzymes like superoxide dismutase, as well as

ingredients like vitamins, carotenoids, and polyphenols(3).

Studies have shown that natural antioxidants, such as polyphenols in green tea, curcumin in turmeric, and resveratrol in grapes, contain potent anti-inflammatory properties. These antioxidants may be found in a variety of foods. They do this by scavenging free radicals and inhibiting the generation of inflammation-related cytokines. Many individuals are under the idea that natural antioxidants relate to fewer negative effects than their synthetic equivalents. Therefore, using natural antioxidants to treat and prevent illness over a longer period is becoming an increasingly desirable option(4).

Regarding food preservation, synthetic antioxidants are often used as preservative alternatives. Some examples of synthetic antioxidants are butylated hydroxytoluene (BHT), butylated hydroxyanisole (BHA), and tert-butylhydroquinone (TBHQ). Chemical procedures are used to manufacture these components in an artificial environment. These chemicals have several positive applications, including extending the shelf life of items and lowering the amount of lipid peroxidation that occurs via reaction(5).On the other hand, synthetic antioxidants in human health have been a contentious subject due to concerns over the stability of these chemicals over an extended period and the potential detrimental effects that they may have. Synthetic antioxidants are crucial in the pharmaceutical and medical sectors due to their durability and efficacy under controlled settings. This is the case even though the difficulties brought to light have arisen(6).

Many people believe that natural antioxidants are superior to synthetic ones because they work in conjunction with the natural defences that the body already has. Curcumin, a naturally occurring antioxidant, has the potential to significantly decrease inflammation by inhibiting the NF-κB pathway itself(7). In addition, there are still concerns over the safety profile of these molecules, even though synthetic antioxidants are reliable and can be delivered in precise quantities. The fact that they might potentially have catastrophic repercussions is the source of these concerns; for instance, research conducted on animals has linked them to the development of cancer. Even though synthetic and natural antioxidants can potentially decrease inflammation and oxidative stress, the decision between the two may be contingent on the patient's requirements and the therapeutic environment(8).

AIM OF THE STUDY

The study aims to compare the efficacy and safety of synthetic versus natural antioxidants in the management of inflammatory diseases.

Objective

To evaluate the antioxidant capacity, anti-inflammatory effects, and potential side effects of synthetic and natural antioxidants in controlling oxidative stress in inflammatory conditions.

Methodology

An experimental examination of synthetic antioxidants took place in this study. Two subgroups of the population known to suffer from inflammatory illnesses, such as rheumatoid arthritis, will be the primary focus of the next inquiry. A synthetic antioxidant was administered to one group of individuals, while a natural antioxidant was administered to another group of subjects. For this investigation, the study included one hundred patients, fifty from each of the two groups, based on inclusion criteria such as age, a confirmed diagnosis, and the absence of any accompanying medical conditions. There had been several opportunities to monitor the varying levels of oxidative stress and inflammatory markers throughout the experiment, which will last six months.

Inclusion Criteria

A total of 100 participants (50 per group) will be selected based on inclusion criteria, such as age, confirmed diagnosis, and absence of confounding medical conditions. The study duration will be 6 months, allowing sufficient time to observe and measure changes in inflammatory markers and oxidative stress levels.

Exclusion Criteria

The following criteria were used to exclude patients from the study:

- Participants with a history of allergic reactions to antioxidants or supplements.
- Individuals currently undergoing treatment with other anti-inflammatory or antioxidant therapies.
- Patients with severe comorbid conditions (e.g., heart failure, chronic kidney disease) that may interfere with the study outcomes.
- Pregnant or lactating women.
- Participants with a history of alcohol or substance abuse.
- Individuals unable to provide informed consent or adhere to study protocols.
- Patients on a strict specialized diet or those taking multivitamin supplements containing antioxidants regularly.

Data Collection

Data were collected at three key intervals: baseline (prior to intervention), at 3 months, and at the conclusion of the 6-month study period. Blood samples were drawn to assess oxidative stress markers, including reactive oxygen species (ROS) and malondialdehyde, alongside inflammatory markers such as C-reactive protein (CRP) and tumor necrosis factor-alpha (TNF-α). These biochemical indicators provided insight into the antioxidant capacity and anti-inflammatory effects over time. Additionally,

clinical evaluations were conducted to monitor changes in disease severity, such as through the Disease Activity Score (DAS28) for participants with rheumatoid arthritis, offering a clear picture of disease progression or improvement. Patient-reported outcomes, including overall well-being and any side effects experienced, were captured using validated quality of life questionnaires. This qualitative data helped assess the safety, tolerability, and efficacy of both natural and synthetic antioxidants. All collected data were anonymized and securely stored for subsequent analysis.

Data Analysis

Data were analysed using SPSS. Descriptive statistics were employed to summarize participant characteristics. A t-test or ANOVA was conducted to compare the efficacy of antioxidants between the two groups over time. Multivariate regression analysis was applied to account for potential confounders, ensuring the accuracy of the results. Statistical significance was determined with a threshold set at $p < 0.05$.

RESULTS

Table 1: Characteristics of Study Participants

Characteristic	Natural Antioxidant Group (n=50)	Synthetic Antioxidant Group (n=50)	p-value
Age (years), mean (SD)	45.2 (7.8)	46.1 (8.3)	0.54
Gender (M/F)	22/28	23/27	0.81
BMI (kg/m²), mean (SD)	25.4 (3.5)	26.1 (4.1)	0.32
Disease Duration (years)	5.2 (1.9)	5.5 (2.2)	0.68
Smoking Status (Yes/No)	14/36	13/37	0.89
CRP (mg/L), mean (SD)	12.5 (4.8)	12.9 (4.5)	0.72
TNF-α (pg/mL), mean (SD)	38.6 (5.2)	37.9 (5.6)	0.45

Table 1 presented the baseline characteristics of participants in both groups. There were no statistically significant differences observed between the natural antioxidant group and the synthetic antioxidant group concerning age, gender distribution, BMI, disease duration, smoking status, or baseline levels of C-reactive protein (CRP) and tumour necrosis factor-alpha (TNF-α). These findings indicated that the two groups were well-matched at the outset of the study, ensuring a fair comparison throughout the intervention.

Table 2: Changes in Oxidative Stress and Inflammatory Markers

Marker	Natural Antioxidant Group (n=50)	Synthetic Antioxidant Group (n=50)	p-value
ROS (Baseline)	8.4 (1.2)	8.5 (1.3)	0.72
ROS (3 months)	5.6 (1.1)	6.4 (1.5)	0.03*
ROS (6 months)	3.9 (0.9)	5.1 (1.2)	0.01*
CRP (Baseline)	12.5 (4.8)	12.9 (4.5)	0.72
CRP (3 months)	9.8 (3.5)	11.3 (4.0)	0.04*
CRP (6 months)	6.7 (2.4)	9.4 (3.1)	0.02*
TNF-α (Baseline)	38.6 (5.2)	37.9 (5.6)	0.45
TNF-α (3 months)	29.4 (4.0)	32.1 (4.8)	0.03*
TNF-α (6 months)	22.5 (3.5)	28.2 (4.1)	0.01*

Table 2 illustrated the changes in oxidative stress (ROS levels) and inflammatory markers (CRP and TNF-α) at baseline, 3 months, and 6 months. Both groups exhibited significant reductions in ROS, CRP, and TNF-α over time; however, the natural antioxidant group demonstrated a more substantial decrease in these markers compared to the synthetic antioxidant group. By 6 months, ROS levels in the natural antioxidant group had decreased by 53.5% ($p = 0.01$), while the synthetic antioxidant group showed a 40% reduction ($p = 0.01$). A similar pattern was observed for CRP and TNF-α levels, with the natural antioxidant group consistently displaying more pronounced improvements.

Table 3: Clinical Outcomes (Disease Activity Score)

Time Point	Natural Antioxidant Group (n=50)	Synthetic Antioxidant Group (n=50)	p-value
DAS28 (Baseline)	5.2 (0.8)	5.1 (0.9)	0.68
DAS28 (3 months)	3.9 (0.7)	4.3 (0.8)	0.04*
DAS28 (6 months)	2.7 (0.6)	3.5 (0.7)	0.02*

Table 3 displayed the changes in Disease Activity Score (DAS28) over time, which was used to assess the severity of inflammatory disease symptoms. Both groups showed notable improvements, with DAS28 scores significantly decreasing from baseline to 6 months. However, the natural antioxidant group demonstrated a more pronounced reduction in disease activity, with an average DAS28 score of 2.7 at 6 months, compared to 3.5 in the synthetic antioxidant group. The differences between the two groups were statistically significant at both the 3-month ($p = 0.04$) and 6-month ($p = 0.02$) time points, indicating a greater therapeutic benefit in the natural antioxidant group.

DISCUSSION

The results of this study revealed that both synthetic and natural antioxidants significantly reduced oxidative stress and inflammation in individuals with inflammatory diseases. Over time, both groups showed marked decreases in reactive oxygen species (ROS), C-reactive protein (CRP), and tumor necrosis factor-alpha (TNF-α), with the natural antioxidant group demonstrating superior efficacy. Notably, by 6 months, ROS levels in the natural antioxidant group decreased by 53.5%, compared to a 40% reduction in the synthetic antioxidant group. A similar trend was observed for CRP and TNF-α levels, with the natural antioxidant group exhibiting more pronounced improvements. Furthermore, the Disease Activity Score (DAS28) indicated a greater reduction in disease activity in the natural antioxidant group, further suggesting that natural antioxidants may offer a more effective therapeutic option for managing disease progression.

These findings are consistent with existing literature on the effects of antioxidants in inflammatory diseases. A study by Tipoe et al.demonstrated that natural antioxidants, particularly polyphenols found in green tea and grapes, significantly reduced oxidative stress and inflammation in patients with rheumatoid arthritis, aligning with the results of this study where natural antioxidants showed superior reductions in ROS levels(9). Similarly, Arulselvanet al.observed that plant-derived antioxidants, such as vitamins C and E, reduced CRP and TNF-α levels in patients with chronic inflammatory conditions, which further supports the findings of the present study(10). However, synthetic antioxidants like N-acetylcysteine (NAC) have shown variable efficacy in managing inflammatory markers. While NAC has been shown to reduce oxidative stress in some studies, it was less effective than natural antioxidants in providing long-term reductions in inflammatory markers, as evidenced by the results in this study.

The comparison between synthetic and natural antioxidants is well-documented in the literature, with both showing therapeutic potential but differing in their mechanisms and long-term effects. Synthetic antioxidants, such as NAC and other pharmacological agents, are designed to target specific biochemical pathways, yet their long-term safety and efficacy remain subjects of ongoing research(11). In contrast, natural antioxidants, with their complex polyphenolic structures and broad bioactivity, affect multiple molecular pathways simultaneously, potentially providing a more comprehensive therapeutic effect(12). These attributes may explain why natural antioxidants exhibited greater efficacy in reducing oxidative stress and inflammation compared to their synthetic counterparts in the present study.

Additionally, the greater improvement in disease activity in the natural antioxidant group corroborates findings from other studies. Research has demonstrated the potential of flavonoid-rich foods, such as berries and citrus fruits, in reducing the severity of inflammatory diseases by inhibiting pro-inflammatory cytokines. This suggests that the therapeutic effects of natural antioxidants extend beyond merely reducing oxidative stress, influencing broader aspects of disease pathology. On the other hand, studies on synthetic antioxidants, like vitamin E, have shown positive effects on oxidative stress but have had limited success in improving clinical outcomes such as disease activity (5).

CONCLUSION

To conclude, this study reinforces the growing body of evidence that natural antioxidants offer significant therapeutic benefits in reducing oxidative stress and inflammation. The results suggest that natural antioxidants may provide a more effective treatment option for managing inflammatory diseases, likely due to their superior antioxidant properties and broader bioactivity. While synthetic antioxidants continue to be valuable in therapeutic settings, their long-term effectiveness in managing inflammation appears to be more limited when compared to natural antioxidants.

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