

# **Study of the Safety and Efficacy of Nature's Rite Sinus Relief to Treat Chronic and Acute Sinusitis: a randomized, double-blinded, placebo-controlled trial**

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## **Abstract:**

**Background:** Due to the increased occurrence of sinus infections, the use of antibiotics is also increasing, thus leading to potential antibiotic resistance. An alternative treatment for sinusitis is widely needed and should be evaluated. The investigational agent tested in this trial is a silver based product in a sinus spray bottle.

**Methods:** Subjects suffering from either chronic or episodic sinusitis were randomly selected to treat their symptoms with either a test or a placebo nasal spray. Subjects rated their daily symptoms on scales ranging from 1 to 9 in order to assess improvement. The treatment was initiated on the first day of the trial and continued for three weeks.

**Results:** Analysis of data from 18 subjects reveals that there were greater reductions of symptoms in the test group than in the placebo group. In the critical first week of the study, the improvement of the test group exceeded the placebo group in all measured symptoms. Greater significance was demonstrated in the progress specifically within the first week and the progress over the entire three weeks of the trial. Mild and equivalent side effects were reported when using both the test and the placebo sprays.

**Conclusions:** The results demonstrate safety and efficacy of the test solution. It was expected that a slight decrease in symptoms would occur in both the test and the placebo groups due to the fact that all of the subjects would be constantly flushing their sinuses with a solution. However, the greater decrease in symptoms that was experienced by the test group subjects may indicate an additional factor affecting the condition. Additionally, subjects with increased compliance during the first week of the treatment showed even greater reductions in symptoms in the test group in comparison to the placebo group, which demonstrates the importance of the designated treatment protocol.

## **Background:**

Sinus infections affect more than 30 million people annually in the United States alone (1). Most sinusitis sufferers have numerous infections per year resulting in very regular antibiotic use. This regular antibiotic use often leads to an escalation in the potency and cost of the prescribed drugs. Prolonged use of antibiotics can also lead to a number of serious side effects including gastrointestinal disturbances, myalgias, and systemic allergic reactions (2). A number of patients who remain unresponsive to other medical interventions resort to reconstructive surgery or surgical removal of nasal polyps, but many patients experience polyp regrowth (1).

The product being tested is administered intra-nasally from a spray bottle according to a protocol and in a concentration covered by U.S. Patent # 6,454,754. The solution is an aqueous colloid of silver. This solution has shown anti-bacterial and anti-fungal properties in laboratory testing. The amount of silver contained in a daily application of the product is below the average daily dietary intake of an average person and therefore does not constitute a health danger (3).

The antibacterial and antifungal properties of silver have long been recognized but previous sinus applications of silver have been limited to drops of silver nitrate or silver sulfadiazene. These previously used solutions were compounded silver and were often in concentrations as high as 5%. This resulted in dosing 10,000 to 100,000 times higher than is required when using a colloidal suspension. This is due primarily to the fact that pure colloiddally suspended silver (not bound to an anion, polysaccharide, or protein) is 100 to 1000 times more antimicrobial than compounded silver salts or silver oxides. Since the earlier applications of silver salts to sinus conditions were so marginally effective, the therapy had to be applied for much greater periods of time. When coupled with the fact that these previous solutions contained 1000 times more silver than the product, the total systemic burden of silver could easily exceed 10,000 times the amount necessary to treat the condition with the product (3).

With the rising popularity of antibiotics in the 50's and 60's, the direct administration of silver salts was largely discontinued. Indeed for several decades, antibiotics were prescribed in copious amounts and seemed to be the simplest answer to the problem. Antibiotics however, tend to kill a particular type of bacteria, leaving room for the surviving bacteria to expand in population. This distortion of the natural fauna of bacteria towards a predominance of antibiotic resistant strains causes future infections to be more difficult to treat. Antibiotics administered orally will affect all of the bacteria within the body, including the desirable indigenous fauna of the body. Since the product is administered intra-nasally in very small amounts, the systemic levels are very low and thus preclude the majority of healthy bacteria from being inadvertently affected (3).

More recently, the suggestion that sinus infections are also caused by fungi which irritate the tissue and leave them vulnerable to bacterial infection has caused an interest in intra-nasally administered antifungals. Due to the antifungal and antibacterial properties of silver, the administration of the product deals effectively with the synergistic alliance by

killing both the bacteria and fungus. Since the active agent is also antifungal, fungus that can grow in the sinus cavity and act as an insulation layer for bacterial biofilms can also be terminated. These fungal growths can provide a lattice structure on which the biofilms develop and thereby keep them out of reach of the subject's immune system. The product being tested kills the fungus and the bacteria allowing a return to a more balanced fauna (3).

The product being tested in this protocol has demonstrated the ability to terminate most sinus infections in several days. Infections that have persisted for more than a year have been terminated in a few weeks. This product has been available as a dietary supplement for more than 10 years during which time more than 300,000 bottles have been sold.

## **Methods:**

Subjects were recruited from local advertisements such as flyers and newspapers and study visits were held at the Klearsen Corporation clinical research department. Subjects were required to have a history of recurring sinus infections, to be currently presenting symptoms, and to be at least 18 years of age. Subjects were disqualified if any antibiotics were used within 2 months prior to beginning the trial, or if any other remedies were used during the trial period. Following a comprehensive screening questionnaire and upon consented enrollment, subjects were randomly assigned to receive a bottle of placebo or test solution to begin using on their first day of the trial. At the first clinic visit, each subject completed a symptom survey and was instructed to apply the nasal spray with one spray in each nostril every 30 minutes throughout the day for the next 21 days. In addition, the subjects were sent home with symptoms surveys to complete daily. The subjects were required to attend weekly visits at the clinic. These weekly visits consisted of a verbal interview, the completion of a weekly symptoms survey, and the weighing of the spray bottle that was assigned to them. At the final visit (visit 4), subjects completed a final weekly symptoms survey, returned their spray bottle, and completed a verbal interview.

The symptoms that were assessed by the subjects were rated on a scale of 1 to 9, 1 representing no symptoms, and 9 representing the worst symptoms possible. The assessed daily symptoms consisted of sleep interference, daily interference, severity of congestion, severity of pressure, severity of tenderness, and overall severity of symptoms due to the sinusitis. In addition, the use of any additional remedies and the occurrence of any adverse events were assessed. The weekly symptoms surveys also included ratings of the overall change in symptoms since the beginning of treatment and the overall satisfaction of the treatment. Subjects were also asked to record the number of applications on a daily basis.

The data was analyzed based on the average reduction in symptoms in the placebo and the test subjects. The averages were compared using a paired t-test to determine significance.

## **Results:**

In order to compare the 8 placebo and 10 test subjects, the differences between various daily and weekly data points were calculated for each symptom parameter that was assessed. After averaging these differences, the difference between the test and the placebo subjects was taken by subtracting the placebo group averages from the test group averages. When the resulting differences were found, the negative numbers represented the comparisons in which the test group had a greater reduction in symptoms than the placebo group. The absolute values of these differences are used to report the results. In order to demonstrate significance, paired t-tests were then applied to all of the symptom parameters as a group for each of the daily and weekly data point comparisons. The most significant comparisons were found to be those within the first week of treatment. Due to the prevalence of self-termination and the differences in duration between individual cases being either chronic or episodic infections, the first week was considered to be the most important week for comparison. The results showed that there were many significant comparisons within the first week. The primary days in which significance was found were days 2, 3, and 4 when compared with day 7 (Table 1). Overall, these results show that there was a greater reduction in symptoms in the test group than in the placebo group in the later part of week 1 in comparison to the early part of week 1. In addition to the comparisons within week 1, significant differences were seen in weekly comparisons. An overall greater reduction in symptoms was seen in the test group in the comparisons between week 3 and weeks 1 and 2 (Table 2).

Comparison (D=day) (W=week)	Sleep Interference	Congestion	Pressure	Tenderness	Overall Severity	Daily Interference	p- value
D7 - D2	1.13	0.65	0.28	1.28	0.85	0.25	<0.01
(D3 to D7) - D2	0.25	0.57	0.13	0.88	0.64	0.00	<0.05
W3 - D2	0.73	0.53	0.55	0.94	0.77	0.17	<0.01
D7 - D3	2.23	0.83	0.70	1.25	0.85	0.75	<0.01
D7 - D4	1.03	0.40	0.73	0.80	0.80	0.60	<0.01
(D5 to D7) - (D2 to D4)	0.76	0.70	0.89	1.18	0.87	0.62	<0.01

**Table 1:** The comparisons are averaged differences of daily or weekly data points along the trial timeline that are used in order to demonstrate the change in symptom parameters. A separate comparison of the same data points was made for each symptom parameter. A paired t-Test was performed on the group of parameters for each comparison in order to demonstrate significance. The value for each symptom parameter represents the difference between the test and the placebo subjects when the test subjects experienced a greater reduction in symptoms over the comparison data points on the timeline. The scale on which the symptoms were rated ranges from 1 to 9.

Comparison (W=week)	Sleep Interference	Congestion	Pressure	Tenderness	Overall Severity	Daily Interference	p-value
W3 – W1	0.32	0.01	0.37	0.07	0.17	0.00	<0.05
W3 – W2	0.90	0.37	0.79	0.33	0.39	0.46	<0.01

**Table 2:** The comparisons are averaged differences of weekly data points along the trial timeline that are used in order to demonstrate the change in symptoms parameters. A separate comparison of the same data points was made for each symptom parameter. A paired t-Test was performed on the group of parameters for each comparison in order to demonstrate significance. The value for each symptom parameter represents the difference between the test and the placebo subjects when the test subjects experienced a greater reduction in symptoms over the comparison data points on the timeline. The scale on which the symptoms were rated ranges from 1 to 9.

The reported side effects were very mild and were reported for both the placebo and the test sprays. Mild headaches were reported by 3 placebo subjects and by one test subject. Slight burning in the throat and nostrils was reported by one placebo subject and by two test subjects. Sneezing was reported by two placebo subjects, nasal irritation was reported by one test subject, and sore throat was reported by one placebo subject and by one test subject. Due to the fact that similar side effects were reported in both the placebo and the test groups, it is mostly likely that most of the side effects are the result of any type of nasal spray rather than the active ingredient in the test spray.

## **Discussion:**

Analysis of the results reveals that the test group experienced greater reductions in symptoms in comparison to the placebo group. The most significant changes were seen as the first week progressed, which is represented by the comparisons between the later and the early days of the first week. In addition, the reductions were greater in the test group when the third week was compared to both the first and the second weeks, which indicates an improvement over the entire trial.

Due to the argument that infections can spontaneously remiss, the first week is the most critical time of the trial, since remission is much less likely. Additionally, since the subjects were considered to be both episodic and chronic cases, the long-term progression of each individual's infection would be different, therefore making the first week the most critical time of the trial. Due to the conclusion that the first week is the critical time of the trial, subject compliance during the first week was separately analyzed by focusing on the subjects that had used greater than 20ml (1/2 bottle) during the first week. When comparing the same data points that were compared in the entire group to the more compliant subjects, the reductions in symptoms in the test group are much greater. Two examples of this, (D7-D2) and (D7-D3), are charted in Tables 3 and 4. The data set of subjects that used greater than 20ml during the first week consists of 6 out of 8 total placebo subjects and 5 out of 10 total test subjects. The improvement in the reduction of symptoms from increased usage compliance is important to recognize in these

preliminary results and should lead to increased regulation of compliance during the first week and throughout the entire study.

Symptom	Complete Data: (D7 – D2)	>20ml in 1 <sup>st</sup> week Data: (D7 – D2)
Sleep Interference	1.13	2.47
Congestion	0.65	1.47
Pressure	0.28	1.53
Tenderness	1.28	2.00
Overall Severity	0.85	1.87
Daily Interference	0.25	1.03

**Table 3:** This table shows the comparison between the symptoms from the complete data set and those from the data set of subjects who used greater than 20ml of solution during the first week of the trial, which is greater. The value for each symptom parameter represents the difference between the test and the placebo subjects when the test subjects experienced a greater reduction in symptoms over the comparison between day 7 and day 2. The scale on which the symptoms were rated ranges from 1 to 9.

Symptom	Complete Data: (D7 – D3)	>20ml in 1 <sup>st</sup> week Data: (D7 – D3)
Sleep Interference	2.23	3.77
Congestion	0.83	1.57
Pressure	0.7	1.60
Tenderness	1.25	1.93
Overall Severity	0.85	1.37
Daily Interference	0.75	1.53

**Table 4:** This table shows the comparison between the symptoms from the complete data set and those from the data set of subjects who used greater than 20ml of solution during the first week of the trial, which is greater. The value for each symptom parameter represents the difference between the test and the placebo subjects when the test subjects experienced a greater reduction in symptoms over the comparison between day 7 and day 3. The scale on which the symptoms were rated ranges from 1 to 9.

A certain amount of reduction in symptoms was expected to be reported by both the test and the placebo groups due to the fact that both groups would be constantly flushing their sinuses with a solution. Nasal irrigation is often recommended to clear the sinuses of mucus (4), which could potentially relieve certain symptoms of sinusitis. However, it would be expected that the solution containing active ingredients would have greater effects on the reduction of symptoms, due to potential action toward the infection.

Therefore, the increased reduction of symptoms reported by the test group leads to greater clinical significance.

Overall, this report of the preliminary results from the study of the safety and efficacy of the product to treat chronic and acute sinusitis concludes that the test solution was more effective in reducing the symptoms of subjects than the placebo solution, particularly during the first week of treatment. Additionally, the results demonstrate that the usage of greater than 20ml of solution during the first week is much more effective in reducing symptoms. The demonstrated efficacy of the test solution and the minimal side effects reported leads to the conclusion that the colloidal silver nasal spray is a safe and effective method for treating chronic and acute sinusitis.

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