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Original Research Article

Efficacy and safety of Koff-N-Cold tablets in patients with allergic rhinitis or seasonal cough and cold: a prospective, randomized, open-label, two-arm clinical trial

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ABSTRACT

Background: Koff-N-Cold is a proprietary polyherbal formulation developed to target both allergic and anti-inflammatory conditions. The objective of this study is to evaluate the efficacy and safety of Koff-N-Cold tablets compared with standard antihistamine therapy in adults with allergic rhinitis or seasonal cough and cold.

Methods: This study is a prospective, randomized, open-label, two-arm clinical trial. Sixty adult subjects (18-65 years) with allergic rhinitis or seasonal cough and cold were randomized in a 1:1 ratio to receive standard therapy [combination of levocetirizine (5 mg) and phenylephrine (5 mg)] for 5 days and Koff-N-Cold tablets for up to 10 days. Efficacy was assessed using symptom severity questionnaires and allergen-specific and anti-inflammatory biomarkers such as serum immunoglobulin E (IgE) and C-reactive protein (CRP) at baseline and Day 10. Safety was evaluated through adverse event monitoring, vital signs, and hematological parameters.

Results: Both treatment groups showed significant improvement in symptom scores from baseline to Day 10. The Koff-N-Cold group showed marked reduction in total symptom scores, serum IgE, and CRP levels by Day 10, therefore achieving improvements greater than the standard levocetirizine and phenylephrine. No adverse events or clinically significant laboratory abnormalities were reported in either group.

Conclusions: Koff-N-Cold tablets were safe and effective in reducing symptoms and inflammatory markers associated with allergic rhinitis and seasonal cough and cold. The findings support Koff-N-Cold as a well-tolerated, evidence-based herbal alternative to conventional antihistamine therapy.

Trial registration: Trial registration number: CTRI/2025/07/092048

Keywords: Allergic rhinitis, Seasonal cough and cold, Herbal medicine, Randomized clinical trial, Immunoglobulin E, C-reactive protein, Safety and efficacy

INTRODUCTION

Seasonal coughs and colds are common respiratory issues, often triggered by viruses (rhinovirus, influenza) or allergies (pollens, molds) during seasonal changes. Allergic rhinitis is an inflammatory nasal condition that is triggered by allergens like pollen, dust, causing sneezing,

a runny or stuffy nose, itchy eyes, and throat.¹ Allergic rhinitis is characterized by symptoms such as nasal congestion, sneezing, sore throat, cough, and fever. These conditions collectively contribute to sleep disturbance, reduced productivity, and impaired quality of life.^{1,2} The underlying pathophysiology involves IgE-mediated hypersensitivity reactions and inflammatory responses,

often accompanied by elevated systemic inflammatory markers such as C-reactive proteins (CRP).³ Seasonal infections may often lead to secondary bacterial infection due to a weak immune system. Seasonal respiratory conditions are managed using antihistamines, nasal corticosteroids, decongestants, or nasal rinses, with immunotherapy for severe cases.^{1,2} While effective in symptom control, these agents may be associated with adverse effects such as sedation, dryness of mucosa, cardiovascular effects, and rebound congestion with prolonged use.^{2,4} Conventional therapies may also not adequately take care of the broader inflammatory component of these conditions.

Herbal and phytomedicinal formulations are potential alternatives due to their multi-target mechanism and favorable safety profile.⁵ Koff-N-Cold is a polyherbal tablet containing standardized extracts of *Ocimum sanctum* (Tulasi) 90 mg, *Adhatoda vasica* (Vasaka) 60mg, *Curcuma longa* (Haridra) 50 mg, *Glycyrrhiza glabra* (Yashtimadhu) 70 mg, and *Terminalia chebula* (Haritaki) 80 mg.

These botanicals are traditionally recognized for their anti-inflammatory, antihistaminic, expectorant, immunomodulatory, and mucoprotective properties.⁶⁻⁹ There are several polyherbal traditional and proprietary blend products available to address some of the respiratory conditions. However, clinical validation with biomarker assessment and comparison of efficacy with standard-of-care anti-histamines like levocetirizine and phenylephrine through well-designed trials is lacking. The present study was undertaken to scientifically evaluate the efficacy and safety of Koff-N-Cold tablets in comparison with a standard antihistamine and decongestant combination in patients with allergic rhinitis or seasonal cough and cold.

METHODS

Investigational product

Koff-N-Cold is designed to provide symptomatic relief while addressing the underlying allergic and inflammatory mechanisms associated with the upper respiratory tract. Each 500 mg tablet contains standardized herbal extracts, formulated based on their established traditional use and documented pharmacological properties.

Informed and ethical consent

This study was conducted in accordance with the principles of Declaration of Helsinki (Ethical Principles for Medical Research Involving Human Subjects, revised by the World Medical Association (WMA) General Assembly, Fortaleza, Brazil, October 2013, International Conference on Harmonization (ICH) recommendation on Good Clinical Practice (GCP), Indian GCP, New Drug and Clinical Trial Rules, 2019, and the Ethical Guidelines for Biomedical Research on Human Participants 2017, issued by Indian Council of Medical Research (ICMR).

The study was designed as a prospective, randomized, open-label, two-arm comparative clinical trial and was conducted at a single clinical center in India. The trial is registered prospectively on CTRI portal on 30/7/2025 (CTRI/2025/07/092048). Ethics Committee Approval was granted by the Institutional Ethics Committee of Sri Venkateshwara Hospital (Protocol Number: RRS/CL/GS/Koff-N-Cold/2025). The Informed Consent Form (ICF) and Patient Information Sheet were also reviewed and approved by the Ethics Committee.

Study design

This was a prospective, randomized, open-label clinical study with two treatment groups in adult volunteers aged between 18 and 65 years. The main objective of the study was to assess the efficacy and safety of Koff-N-Cold tablets in individuals with allergic rhinitis or seasonal cough and cold. A total of 60 eligible subjects were equally randomized into two groups (Figure 1).¹⁰

Subject selection for study

Sample size calculation

The sample size for this randomized controlled clinical trial was calculated using the following formula for comparing the mean difference between two independent groups:

$$n = (Z_{1-\alpha/2} + Z_{1-\beta})^2 (\sigma_1^2 + \sigma_2^2) / (\mu_1 - \mu_2)^2$$

$$= ((1.96 + 0.85) / (6 - 4))^2 (2.34^2 + 2.52^2)$$

$$n = 23 + 3(10\%) = 26$$

Where:

n=required the sample size per group (in this case, per arm).

$Z_{1-\alpha/2}$ =Z-score for the desired level of significance (α).

$Z_{1-\beta}$ =Z-score for the desired power of the test ($1-\beta$).

σ_1 and σ_2 =standard deviation of the outcome variable in respective groups.

$\mu_1 - \mu_2$ (δ)=the minimum clinically significant difference

$n_1 = 23$

Considering a dropout rate of 10%, then $n_1 = 26$

Based on the above assumptions, the calculated minimum sample size was 23 participants per group. To compensate for an anticipated 10% dropout rate, the sample size was increased to 26 participants per group. For operational feasibility and to ensure adequate statistical power, the

sample size was further rounded up to 30 participants per group.

Accordingly, the study enrolled a total of 60 participants, with 30 participants allocated to the intervention arm and 30 participants to the control arm. This sample size was considered sufficient to achieve the desired statistical power while accounting for potential participant attrition during the study period.

Randomization

Participants meeting all eligibility criteria were randomly allocated to either treatment group in a 1:1 ratio using a computer-generated randomization schedule. The study was open-label; therefore, participants and investigators were aware of the assigned treatment after randomization.

Randomization and allocation concealment were intended to support an objective and unbiased assessment of the safety and efficacy of Koff-N-Cold tablets compared with the standard antihistamine in patients with allergic rhinitis or seasonal cough and cold.

Inclusion criteria

Participants aged between 18 and 65 years were recruited. Eligible participants presented with seasonal cough and cold, and allergic rhinitis. Subjects experiencing symptoms such as a runny nose or low fever were included in the study.

Exclusion criteria

Subjects with pre-existing severe systemic illness requiring long-term medication or clinically significant uncontrolled co-morbid conditions that, in the investigator's judgement, could have compromised subject safety or interfered with study outcomes were excluded. Individuals with oncological, neurological, vascular, or other systemic disorders that could affect efficacy assessments were not eligible. Additional exclusion criteria included recent participation in treatment involving approved or investigational health supplements, inability to understand or comply with study procedures due to psychiatric or cognitive impairment, known hypersensitivity to any component of the investigational product or study procedures, and the presence of significant medical conditions such as cardiovascular disease, uncontrolled diabetes, or immunosuppressive disorders. Pregnant or breastfeeding individuals and subjects with chronic infectious conditions such as tuberculosis, pneumonitis, or bronchitis were also excluded.

Treatments, grouping, and visit schedule

Eligible participants were randomly assigned to one of the two treatment groups in a 1:1 ratio. Group A received standard treatment (Levocetirizine [5 mg] + Phenylephrine

[5 mg]) while Group B received the Koff-N-Cold Tablet (500 mg). The subjects in Group A were instructed to take one tablet twice daily for five days, and the subjects in Group B were instructed to take two tablets twice daily for three days, followed by one tablet twice daily for the next seven days.

The study was conducted over a total duration of 10 days for each subject. The study included three scheduled visits, viz., a baseline visit (Visit 1), an intermediate assessment visit (Visit 2), and an end-of-study visit on Day 10 (Visit 3). A follow-up was carried out at Day 20. Clinical evaluations, safety assessment, and laboratory investigations were performed according to the protocol-defined schedule at each visit.¹⁰ Data analysis was conducted according to predefined statistical methods.^{2,3}

Subjects were instructed to follow the prescribed dosing regimen throughout the treatment period, and adherence was evaluated based on participant feedback recorded in Case Report Forms.

Efficacy and safety variables

Primary endpoints

Primary endpoints included evaluation of changes in the severity of symptoms of allergic rhinitis and Acute Respiratory Infections (ARIs) like, cough, cold, sneezing, running nose, and fever from the baseline visit to day 10, using symptomatic questionnaires.¹⁻³

Secondary endpoints

Assessing the safety of Koff-N-Cold tablets through hematological evaluations conducted at screening and on Day 10, along with continuous monitoring of any adverse events or health-related concerns throughout all study visits. Additionally, the effect of the tablet on participants' quality of life was evaluated using standardized Quality of Life questionnaires administered during visits 1, 2, and 3.¹⁰

Biochemical endpoints and biomarkers analysis

Biochemical endpoints included a panel of biomarkers selected to evaluate the functional impact of Koff-N-Cold tablets on allergic rhinitis and acute respiratory illness. Biomarkers IgE and CRP were selected based on their role in the pathophysiology of allergic and respiratory conditions.^{2,3,10,11} They were measured at baseline (Visit 1) and at Day 10. All biomarker assessments were conducted using validated immunoassay techniques.

Serum samples were collected, centrifuged, and stored at -20°C until analysis. All assays were performed in accordance with validated procedures with appropriate calibration and controls. The units of measurement and assay sensitivity were consistent with clinical laboratory standards to ensure accuracy and reproducibility of the results.

Safety measurements

Safety was evaluated through systematic monitoring of adverse events reported by participants during scheduled visits. The events were appropriately classified, summarized, and documented. Clinical laboratory evaluations were performed, including routine blood evaluations and regular assessment of vital signs such as systolic and diastolic blood pressure, pulse rate, respiratory rate, and body temperature to ensure overall subject safety throughout the study.

Disposition of patients

A total of 68 subjects were screened from a single center to enroll 60 subjects into the study. Out of the 60 subjects who were enrolled, 58 subjects completed the study, and 2 subjects were lost to follow-up (Figure 2).

Statistical analysis

Independent t-test or Mann-Whitney U test were used for analyzing comparison between group A and group B, while paired t-test or Wilcoxon Signed-Rank test were applied for within-group analysis. A $p < 0.05$ was considered statistically significant. For categorical data, the chi-square or Fisher's exact test was used and described in frequency and percentages. Adverse events and serious adverse events were analyzed individually and were described as percentages.

RESULTS

Demographic and baseline characteristics

The baseline demographic characteristics were comparable between the two treatment groups in both the full analysis set (FAS) and per protocol set (PPS) populations. In the FAS population, the mean age at screening was 44.90 ± 13.75 in Group A and 44.40 ± 11.72 in Group B, with no statistically significant difference between groups ($p = 0.7224$). Age ranges and confidence intervals were comparable, which indicates a balanced age distribution at baseline. The mean height at screening was 166.53 ± 9.73 cm in Group A and 163.43 ± 9.27 cm in Group B, with no significant difference ($p = 0.1442$) (Table 1) between the groups.

The mean body weight at screening was similar between Group A (60.80 ± 6.42 kg) and Group B (60.20 ± 5.07 kg) ($p = 0.6897$). Throughout the study, body weight remained stable at both Day 5 and Day 10, with only minimal changes from baseline that were similar across both treatment groups ($p > 0.05$) (Table 1).

The mean baseline BMI values were also comparable between Group A (21.92 ± 1.43 kg/m²) and Group B (22.59 ± 1.60 kg/m²) ($p = 0.0955$). BMI remained stable throughout the study with no statistically significant differences observed between groups at Day 5 or Day 10,

and no clinically meaningful changes from baseline ($p > 0.05$) (Table 1).

Similar findings were observed in the PPS population. The mean age, height, body weight, and BMI at screening were well balanced between Group A and Group B, with no statistically significant group differences ($p > 0.05$). Across all post-baseline visits, weight and BMI remained stable, and the changes from screening to Day 5 and Day 10 were minimal and comparable between the groups.

Primary efficacy outcomes

Change in overall symptom score

The primary efficacy analysis evaluated the effectiveness of the investigational product compared with the control. In the FAS population, the Day 0 (baseline) total symptom scores were slightly higher in Group B than in Group A, with a statistically significant difference observed between the groups. Despite this baseline imbalance, both the treatment groups showed a marked reduction in symptom severity by Day 5. At this point, a statistically significant difference was observed between the two groups, with Group A showing a greater reduction in total symptom scores compared with Group B. The adjusted mean analysis supported a numerically greater improvement in Group A at Day 5, although statistical significance was marginal after adjustment.

Continued improvement in symptom scores was observed in both groups by Day 10, with mean values merging and no statistically significant difference observed. Adjusted mean comparisons at Day 10 similarly showed no significant difference between the two groups, which indicates comparable overall symptom control at the end of treatment.

The change from baseline showed a statistically significant improvement in symptom scores by Day 5 in both groups, with a significantly greater early reduction observed in Group A. By Day 10, the overall change from baseline was substantial and highly significant within each group, with no meaningful difference between the treatment arms, which indicates comparative cumulative efficacy.

Serum IgE levels were assessed as an objective biomarker of allergic activity. In the FAS population, the baseline serum IgE concentrations were comparable between group A and Group B. By Day 10, both groups demonstrated a significant reduction in serum IgE levels from the baseline. The magnitude of reduction was similar between the groups, with no statistically significant intergroup difference, while within-group reductions were highly significant ($p < 0.0001$) (Figure 3).

Serum CRP levels were evaluated to assess systemic inflammation. The baseline CRP concentrations were comparable between the two groups in the FAS population. At Day 10, the mean CRP concentrations were

significantly reduced from baseline in both the treatment groups. The extent of reduction did not differ significantly between Group A and Group B, while within-group changes were highly statistically significant ($p < 0.0001$), indicating a marked anti-inflammatory effect in both groups (Figure 4).

The primary efficacy analysis showed significant improvement in symptom severity and objective inflammatory biomarkers in both treatment groups. An earlier symptomatic response was observed in group A, and comparable overall efficacy between the groups by the end of the treatment period.

Individual symptom analysis

Analysis of individual symptoms demonstrated consistent improvement across all assessed parameters in both treatment groups. The individual symptom severity was assessed using a standardized 0-4 ordinal scale at baseline (Day 0), mid-treatment (Day 5), and end of treatment (Day 10), and the results are given in Figure 5 A-G.

At baseline, both the treatment groups exhibited moderate to severe symptom severity across all domains, indicating a high and comparable symptom burden prior to treatment. By Day 5, both groups demonstrated clinically meaningful improvement across all individual symptoms, with a shift from higher severity scores to mild and moderate categories. In several symptoms, an earlier improvement was observed in Group A at Day 5, while Group B showed a comparable trend.

By Day 10, most of the symptoms have largely resolved in both groups. The majority of participants reported either complete resolution or only mild residual symptoms across all individual symptom domains, with no participants reporting moderate or severe symptoms.

Ocular symptoms followed a similar pattern. The baseline ocular symptom severity was comparable between the groups. By Day 5, both groups showed significant improvement with a greater reduction observed in Group A. By Day 10, ocular symptoms were minimal in both groups, with no clinically meaningful differences between treatments.

The analysis of individual symptom scores showed a consistent and progressive reduction in symptom severity from baseline to Day 10 in both treatment groups, supporting the broad symptomatic efficacy of the study interventions.

Secondary efficacy results

In the FAS population, the baseline quality-of-life scores were comparable between the two treatment groups, with no statistically significant differences observed. Both groups have revealed a clinically progressive improvement

in quality-of-life scores by Day 5, with no significant inter-group differences.

Substantial improvement in quality of life was observed in both the treatment groups. The magnitude of improvement from baseline was large and highly statistically significant within each group, while between-group comparison demonstrated no statistically significant differences, indicating comparable enhancement in overall well-being.

Efficacy conclusions

In both the FAS and PPS populations, treatment with Koff-N-Cold tablets resulted in statistically significant improvements in clinical symptoms of allergic rhinitis and seasonal cough and cold. Despite minor baseline variations, both groups revealed substantial symptom reduction over time, with nearly identical magnitudes of improvement by Day 10. The comparable decrease in serum IgE levels across the groups indicates effective attenuation of allergic inflammation, supporting the efficacy of Koff-N-Cold, comparable to standard antihistamines. Similarly, the significant reduction in serum CRP levels in both groups reflects a strong anti-inflammatory response, which further confirms the therapeutic benefit of Koff-N-Cold. The parallel trends observed in both the analysis populations affirm the robustness and consistency of these findings, showing that Koff-N-Cold provides clinically meaningful and well-tolerated relief in managing symptoms associated with allergic rhinitis and seasonal cough and cold.

The results showed improvements in both symptom scores and biomarkers of allergic inflammation. During the 5-day treatment, participants taking Koff-N-Cold showed a mean symptom score reduction of -17.53 ± 1.66 , while the standard of care group had a reduction of -16.63 ± 1.19 . By Day 10, both serum IgE and CRP levels showed significant and similar reductions in the two treatment groups. Koff-N-Cold group had a substantial decrease in serum IgE of -25.27 ± 5.55 IU/mL, while the standard-of-care group showed a similar reduction of -25.60 ± 5.42 IU/mL from baseline, indicating equivalent anti-allergic effects. Similarly, CRP levels also declined significantly in both groups, with a mean reduction of -2.01 ± 0.50 mg/L in Group A and -1.94 ± 0.49 mg/L in the standard-of-care group by Day 10. These results suggest that the investigational product provided significant relief from clinical symptoms and effectively modulated systemic inflammatory responses.

Safety and tolerability

No adverse events (AEs), serious adverse events (SAEs), deaths, or other clinically significant safety events were reported in either the Koff-N-Cold group or the standard treatment group throughout the study period. All participants completed the study without treatment-related intolerance, discontinuations, or safety concerns, which indicates good overall tolerability for both interventions.

Safety was assessed at baseline with clinical laboratory assessment, including complete hematological parameters.

Values were comparable between treatment groups. Across the study period, hematological indices including red blood cell count, white blood cell count and differentials, platelet count, erythrocyte sedimentation rate and packed cell volume remained stable, with no clinically meaningful or statistically significant changes observed from baseline to day 10 in either group.

All measured values remained within normal physiological ranges.

Vital signs, including systolic and diastolic blood pressure, heart rate, pulse rate, respiratory rate, and the body

temperature, monitored at baseline, during treatment, and at the end of the study were comparable between the treatment groups.

Across all post-baseline assessments, vital signs remained stable, with no clinically meaningful or statistically significant changes observed within or between groups.

No abnormal findings were detected on physical examination, and no safety-related clinical observations were reported.

Overall, the absence of reported adverse events and the stability of laboratory parameters support the favorable safety profile and good tolerability of Koff-N-Cold tablets when administered according to the study protocol.

Table 1: Baseline demographic and clinical characteristics-FAS.

Treatment schedule	Parameter	Group A, (n=30)	Group B, (n=30)	P value
Screening	Age (in years)	44.90±13.75	44.40±11.72	0.7224 ^{@@}
	Range (Min/Max)	27.00, 64.00	26.00, 65.00	
	Median	43.00	47.00	
	CI	39.76, 50.04	40.02, 48.78	
Screening	Height (cm)	166.53±9.73	163.43±9.27	0.1442 ^{@@}
	Range (Min/Max)	154.00, 180.00	152.00, 180.00	
	Median	165.50	159.00	
	CI	162.90, 170.17	159.97, 166.89	
Screening	Weight (Kg)	60.80±6.42	60.20±5.07	0.6897 [#]
	Range (Min/Max)	51.00, 72.00	52.00, 70.00	
	Median	60.50	60.00	
	CI	58.40, 63.20	58.31, 62.09	
Day 5	Weight (Kg)	60.73±6.56	60.16±5.02	0.8015 ^{@@}
	Range (Min/Max)	50.90, 72.30	51.90, 69.80	
	Median	60.35	59.90	
	CI	58.28, 63.18	58.28, 62.04	
Day 10	Weight (Kg)	60.69±6.54	60.11±5.00	0.8072 ^{@@}
	Range (Min/Max)	50.80, 72.10	51.70, 69.70	
	Median	60.25	59.65	
	CI	58.25, 63.13	58.24, 61.98	
Screening	BMI (kg/m ²)	21.92±1.43	22.59±1.60	0.0955 [#]
	Range (Min/Max)	19.05, 24.84	19.44, 25.20	
	Median	21.84	22.74	
	CI	21.39, 22.46	21.99, 23.18	
Day 5	BMI (kg/m ²)	21.89±1.43	22.57±1.63	0.0892 [#]
	Range (Min/Max)	19.08, 24.88	19.17, 25.33	
	Median	21.63	22.80	
	CI	21.36, 22.42	21.97, 23.18	
Day 10	BMI (kg/m ²)	21.88±1.42	22.55±1.61	0.0895 [#]
	Range (Min/Max)	19.06, 24.92	19.23, 25.29	
	Median	21.69	22.82	
	CI	21.34, 22.41	21.95, 23.15	

^{@@}P value is calculated by using the Mann-Whitney U test (p<0.05 is statistically significant); [#]P value is calculated by using an independent t test (p<0.05 is statistically significant); *P value is calculated by using paired t test (p<0.05 is statistically significant); **P value is calculated by using the Wilcoxon Signed- Rank test (p<0.05 is statistically significant); SD-Standard deviation, Min-Minimum, Max-Maximum, CI-Confidence intervals.

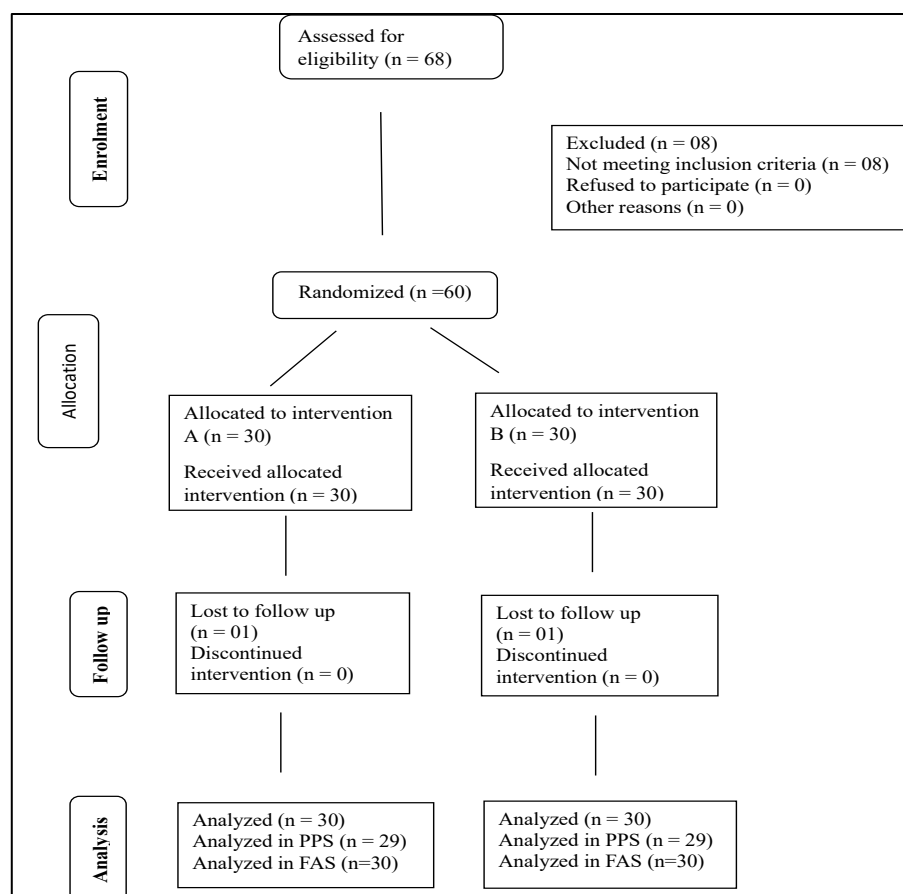


Figure 1: CONSORT flowchart of study design.

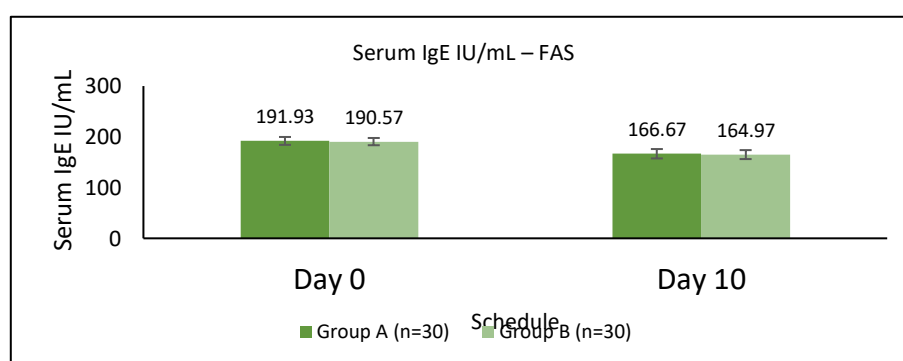


Figure 2: Serum IgE IU/mL-FAS.

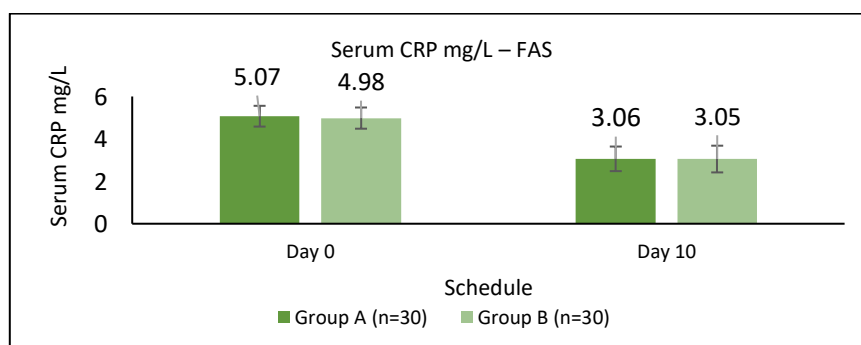


Figure 3: Serum CRP mg/L-FAS.

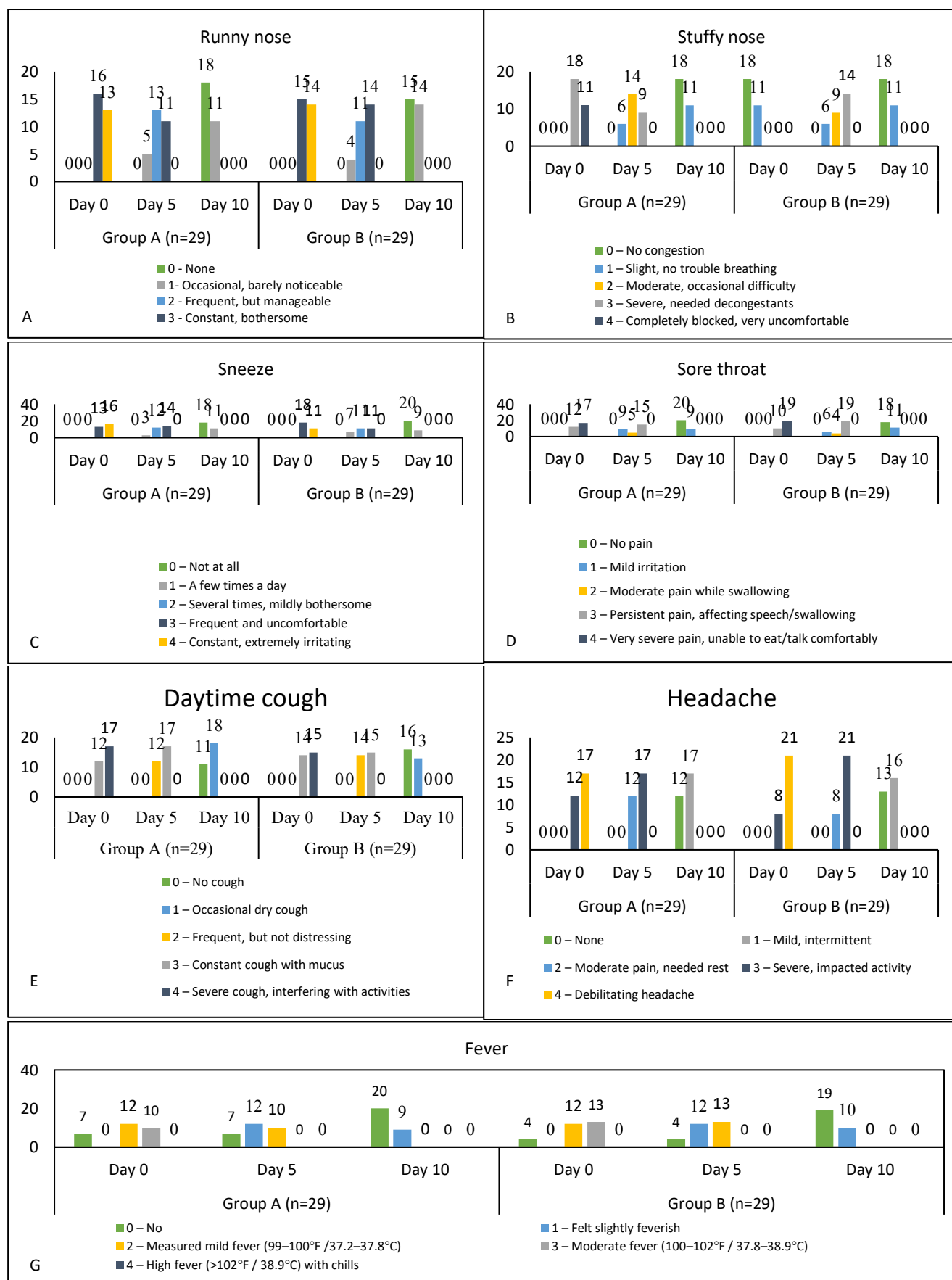


Figure 4: Individual symptom scores. A) runny nose b) stuffy nose c) sneeze d) sore throat e) daytime cough f) headache g) fever.

DISCUSSION

A prospective, randomized, two-arm active-comparator design enables systematic evaluation of the clinical efficacy, safety, and inflammatory biomarkers of Koff-N-Cold. Conventional antihistamine therapy is typically administered for 5 days, whereas Koff-N-Cold was evaluated for 10 days to assess sustained symptom control with a reduced-dose regimen during the latter part of treatment. Day 5 outcomes were compared between groups, with participants subsequently followed through Day 10 to evaluate persistence and progression of therapeutic response. The open-label design was considered appropriate due to differences in the appearance and dosing characteristics of the interventions.

A study-specific symptom assessment tool, together with objective biomarkers such as serum IgE and CRP, provides complementary measures of clinical and inflammatory response.

The standard treatment, fixed-dose combination of Levocetirizine (a second-generation H₁-antihistamine) and Phenylephrine (a nasal decongestant), and similar products have shown to provide rapid and meaningful relief from allergic rhinitis symptoms.¹² However, they can cause sedative effects, agitation, insomnia, headache, and palpitations,¹⁵ which can limit their use. Alternative medications are preferred and prescribed; there is not enough evidence on their efficacy on symptom relief correlated with biomarker assessment.

Present study's 10-day duration and biomarker changes (IgE decrease approx. 25 IU/ml and CRP approx. 2 mg/l) suggest that the herbal formulation achieves meaningful biological changes at a relatively similar timeframe. The observed reduction in mean serum IgE by approx.

The 25 IU/mL supports the idea that allergic rhinitis can decrease IgE levels over time. Total serum IgE levels showed a slower rate of decline, which is expected given that IgE reflects chronic immune activation and production by long-lived plasma cells. Accordingly, normalization of IgE typically occurs over a longer time course than CRP, and the differential temporal response does not indicate ongoing acute inflammation. The ability of the botanical combination in Koff-N-Cold formulation to reduce IgE and CRP levels in 10 days aligns with the anti-inflammatory and immunomodulatory effects reported for standard antihistamines.

The significant improvements observed in symptom scores, along with the reductions in serum IgE and CRP levels in patients treated with Koff-N-Cold, can be explained by the pharmacological mechanisms associated with its herbal constituents. Network pharmacology and molecular docking analysis suggest that the bioactive constituents, such as quercetin, luteolin, kaempferol, glycyrrhizin, and compounds from *Adhatoda vasica*, interact with multiple molecular targets, including AKT1,

PTGS2, MMP-2, MMP-9, EGFR, SRC, and STAT3, which are known to regulate inflammatory signaling, immune responses, and airway remodeling. Modulation of key pathways such as PI3K-Akt, NF- κ B, MAPK, IL-17/STAT3, and TGF- β -associated signaling provides a mechanism for the observed decline in CRP, reflecting reduced systemic inflammation, while downregulating IgE-associated immune activation supports the gradual reduction in serum IgE levels over the 10-day period. Molecular dynamics simulation further supports the stability of phytoconstituents binding to inflammatory and remodeling targets, suggesting a sustained biological activity rather than a temporary receptor interaction. Koff-N-Cold formulation provides effective symptom relief and biomarker improvement through a multitarget, immunomodulatory approach, offering efficacy comparable to standard antihistamine therapy while addressing broader inflammatory pathways involved in allergic rhinitis and seasonal cough and cold.¹⁶

The standard therapy offers faster onset of symptomatic relief, while Koff-N-Cold provides a progressive the end of the study.

Several prior clinical and experimental studies evaluating herbal and polyherbal formulations in allergic rhinitis have reported outcomes comparable to conventional antihistamines, particularly in terms of symptom relief and reduction of inflammatory mediators.^{17,18} Botanical formulations with anti-inflammatory, antihistaminic, and immunomodulatory constituents have shown significant reduction in nasal symptom scores and inflammatory cytokines. These effects are attributed to multi-target mechanisms such as cell stabilization, inhibition of histamine release, antioxidant activity, and downregulation of pro-inflammatory pathways.¹⁷⁻¹⁹ The comparable symptom reduction observed in the present study aligns well with these findings.

Limitations

The symptom score used in this study is a study-specific customized symptom assessment tool developed to evaluate the severity of allergic rhinitis and seasonal cough and cold symptoms based on the study objectives and clinical relevance. Thus, no published external validation reference is available. Continued treatment with Koff-N-Cold resulted in significant reductions in symptom scores, serum IgE, and CRP levels by day 10, demonstrating a sustained therapeutic response and superior overall efficacy compared with standard therapy. The study population included patients with allergic rhinitis or seasonal cough and cold, but did not categorize them by the type of allergen, whether allergic triggers, or severity. Such stratification may reveal differential responses.

CONCLUSION

The randomized comparative study indicate that Koff-N-Cold tablets provide clinically meaningful improvement in

symptoms of allergic rhinitis and seasonal cough and cold, with efficacy comparable to the standard anti histamine treatment. The significant reductions observed in symptom scores, serum IgE, and CRP levels over a 10-day period suggest effective modulation of both allergic and inflammatory pathways. This study provides strong evidence that Koff-N-Cold tablets significantly reduced both symptom burden and key biomarkers of allergic inflammation in a 10-day treatment period. The formulation was well tolerated, with no treatment-related adverse events or clinically significant laboratory abnormalities. These findings support the potential of Koff-N-Cold as a safe, evidence-based polyherbal formulation for the management of allergic rhinitis and seasonal cough and cold.

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Conflict of interest: None declared

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