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Safety and Efficacy Study of EqualsTwo® Cold Relief Roll-on in Infants and Toddlers

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ABSTRACT

Background: Acute upper respiratory tract infections are highly prevalent in infants and toddlers, causing nasal congestion, sleep disruption, and caregiver distress. Pharmacologic cold remedies are not recommended in this age group, creating a need for safe, natural alternatives.
Objectives: To assess the safety, tolerability, and efficacy of the EqualsTwo® Cold Relief Roll-on (investigation product) in reducing cold symptoms and improving comfort in infants and toddlers aged 0–36 months.
Methods: This prospective, open-label study enrolled 37 infants and toddlers with acute cold symptoms. Participants received topical application of the investigation product for 7 days. Efficacy and tolerability endpoints included changes in Total Nasal Symptom Score (TNSS), time to onset and overall relief of symptoms through Visual Analog Scale (VAS), caregiver-reported outcomes, dermatological assessment, and absorption profile. Safety was monitored through adverse event reporting.
Results: All enrolled pediatric patients completed the study. TNSS scores declined rapidly and significantly ($p<0.0001$), reaching complete symptom resolution within 3 hours and remained low through Day 7. Overall relief occurred in >80% within half an hour and 100% within 3 hours. Caregivers reported improvements in comfort, sleep quality, and ease of breathing, with 100% overall satisfaction. The investigation product was rapidly absorbed, non-greasy, and well tolerated, with no adverse events reported.
Conclusions: The investigation product is safe, well tolerated, and effective in providing rapid, sustained relief of acute cold symptoms in infants and toddlers, offering a natural and practical solution for management of cold symptoms in pediatrics.

Keywords: Common Cold, Eucalyptus oil, Mentha piperita, Nasal congestion, Rosmarinus officinalis, Upper respiratory tract infection

INTRODUCTION

Acute upper respiratory tract infections (URTIs), commonly called colds, are among the most frequent illnesses in children and account for more visits to healthcare providers.[1] As young children have immature immune defences and are

frequently exposed to pathogens through childcare and siblings, colds occur repeatedly. Young children, especially those under 2 or 3 years, commonly experience frequent colds, sometimes as many as 8 to 10 colds per year before age 2, while infants may develop up to seven colds in their first year of life.[2] Symptoms include nasal congestion, sneezing and cough, irritability, decreased appetite and difficulty sleeping. These disturbances not only affect infants' feeding and growth but also disrupt parental sleep and well-being. Even after age six, children are still likely to contract 6–8 colds annually.[3]

Management of common cold relies on symptomatic relief and supportive care. Guidelines recommend maintaining hydration, using paracetamol or ibuprofen for fever, and employing saline nasal drops or honey (for children over 12 months) to soothe cough.[4] Over the counter (OTC) cough and cold medicines are not recommended for young children because they do not work well and can cause serious side effects. Public health agencies advise against giving these medicines to children under 12 years, and the American Academy of Pediatrics and U.S. Food and Drug Administration caution that OTC cough and cold products must not be used in infants and toddlers under two. [5,6] Consequently, caregivers have limited options for relieving infants' cold symptoms, and many turn to non-pharmacologic remedies such as humidified air, suctioning and gentle massage. The lack of safe, effective treatments highlights the need for alternative approaches.

The desire to alleviate cold symptoms through non-pharmacological formulations has spurred interest in herbal and traditional remedies. A systematic review of plant derived substances used in OTC cough and cold products emphasizes that URTIs imposes a substantial economic burden yet lacks a single effective treatment.[7] Scientific investigations into their mechanisms have shown that menthol (a major constituent of peppermint oil) activates cold sensitive Transient Receptor Potential Melastatin 8 (TRPM8) receptors in nasal mucosa, suppressing respiratory reflexes and thereby reducing irritation and cough.[8,9] Menthol may also inhibit Transient Receptor Potential Ankyrin 1 (TRPA1) channels, conferring an analgesic effect.[10] Eucalyptol (from eucalyptus oil) likewise activates TRPM8 and inhibits TRPA1 while downregulating Purinergic Receptor P2X, Ligand-Gated Ion Channel 3 (P2X3) receptors, which together help reduce cough, pain and airway irritation.[7,11] These properties may offer benefits for nasal congestion and upper respiratory discomfort, although controlled studies remain limited. Coconut oil is widely used as a carrier oil due to its gentle emollient properties and rapid dermal absorption, making it suitable for use on delicate infant skin.

Given the high burden of common colds in both infants and toddlers, and the paucity of approved pharmacologic treatments, natural products containing essential oils are an attractive option for symptom relief. The EqualsTwo® Cold Relief Roll on (investigation product) combines Eucalyptus globulus oil (12% w/w), Rosmarinus officinalis (rosemary) oil (1.0% w/w) and Mentha piperita (peppermint) oil (5.0% w/w) in a Cocos Nucifera oil (0.5% w/w) base. Each ingredient offers complementary mechanisms: eucalyptus and peppermint oils have been shown to provide sensory relief of congestion via activation of TRPM8 channels and inhibition of pro irritant receptors; rosemary oil contributes anti-inflammatory and antimicrobial properties that may reduce local inflammation; and the lightweight coconut oil base that supports efficient skin absorption while minimising surface residue. Parents/caregivers in our practice frequently report using essential oil formulations to soothe congested infants and toddlers, yet robust evidence for their efficacy and safety in this specific pediatric population is lacking. Therefore, this study aimed to evaluate the safety, tolerability, and symptomatic outcomes associated with the

use of investigation product formulation in a pediatric population aged 0–36 months.

MATERIALS & METHODS

Study Design and Setting: This open-label, interventional, prospective, single arm study was conducted by NovoBliss Research Private Limited, Gandhinagar at 2 sites for a duration of 7 days to evaluate the safety, tolerability, and efficacy of the investigational product in infants and toddlers presenting with acute cold symptoms.

Study Population: A total of 37 infants and toddlers aged 0 to 36 months were enrolled. All enrolled subjects completed the study. Eligible participants included infants and toddlers with acute cold symptoms such as nasal congestion, sneezing, nasal itching, or rhinorrhea, and otherwise deemed healthy by a paediatrician. Exclusively breast-fed infants up to six months of age were also eligible. Key exclusion criteria were chronic respiratory illness, congenital anomalies, neuromuscular disorders, cystic fibrosis, history of hypersensitivity to similar products, requirement of ventilatory support, or concomitant medications likely to interfere with the study product. Written informed consent was obtained from the parent or legal guardian of each participant prior to enrolment.

Study Objective: The primary objective of the study was to assess the in-use safety, tolerability, and efficacy of the investigational product in providing relief from acute cold symptoms, including nasal congestion and associated discomfort, while also promoting calmness and restful sleep, in infants and toddlers.

Intervention: Caregivers were instructed to gently apply the investigation product over the chest, neck, back, and soles of the feet. The investigation product was used as needed, or as directed by the pediatrician, for a total duration of seven consecutive days.

Study Procedures and Visits: The study consisted of three visits over a seven-day period. At baseline (Day 1), screening, enrolment, baseline assessments, and the initiation of treatment were conducted. 1st follow-up (Day 2) comprised a telephonic follow-up to assess symptomatic relief and caregiver-reported outcomes. Second follow-up (Day 7 ± 1) served as the end of study visit, during which safety and efficacy assessments were completed. Throughout the study, caregivers maintained a daily diary documenting the timing of roll-on application, perceived symptomatic relief, sleep quality, and tolerability. Diaries and remaining products were reviewed at the end-of-study visit to assess compliance.

Outcomes Measured: Efficacy was evaluated primarily through changes in acute cold symptoms using the caregiver-reported modified Total Nasal Symptom Score (TNSS), adapted for infant behavioural observation which assessed nasal congestion, sneezing, nasal itching, and rhinorrhea on a 4-point scale. Overall relief was further assessed using a caregiver-reported Visual Analogue Scale (VAS) pertaining to the tolerability of the investigation product. A subjective perception questionnaire was administered to evaluate calming effects, sleep quality, ease of breathing, and overall satisfaction with the investigational product maintained by caregivers throughout the study. Absorption and clinical acceptability were evaluated using the tissue-blotting (absorbent paper) test to assess residual surface oiliness and the time to perceived absorption following application. The tissue absorbent test graded the greasiness on 5 scale (1 = No greasiness, 2 = Slightly greasy, 3 = Moderately greasy, 4 = Severely greasy, 5 = Very severe greasy) which was later evaluated by trained study staff, indicating the absorption power of investigation product into the skin within 5 mins of application.

Safety was assessed through systematic monitoring, Subjective Perception Questionnaire and documentation of adverse events, alongside investigator-performed dermatological examinations for local tolerability (e.g., erythema, rash, irritation) at scheduled study visits.

Ethical Considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice (GCP) guidelines. The protocol was approved by ACEAS, an Independent Ethics Committee. This clinical study was registered at CTRI (Clinical Trial Registry of India) under the trial registration number: CTRI/2024/03/063975 dated 11 Mar 2024.

Statistical Analysis

Data was collected via validated and structured case report forms and analyzed using SPSS version 25. Descriptive statistics were used to summarize demographic and baseline characteristics. Changes in TNSS and VAS scores were analyzed using appropriate statistical tests. A two-sided p-value of <0.05 was considered statistically significant.

RESULT

Baseline Characteristics

A total of 37 infants and toddlers with normal vital signs were enrolled in the study, and all the participants completed the study. Among all the participants, 62.2% were girls and 37.8% were boys. The mean age was 17.8 (±11.11) months, with participants ranging from 0.9 months to 35 months. The detailed demographic characteristics are presented in Table 1.

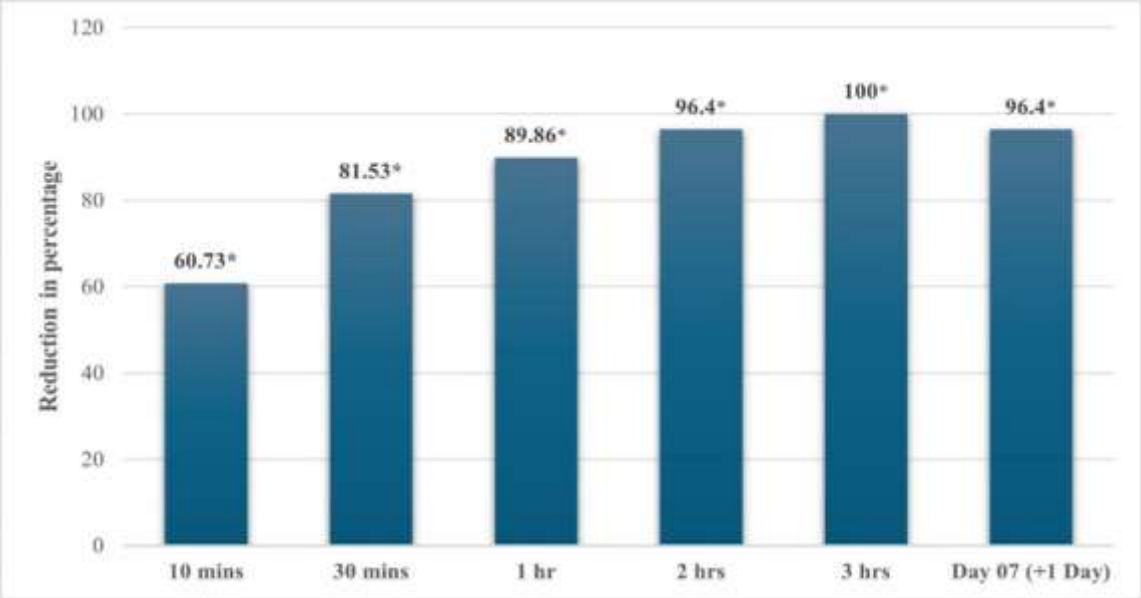
Table 1. Baseline demographic and clinical characteristics of study participants (N = 37)

Parameter	Statistic	Values
Gender, n (%)	Girl	23 (62.16)
	Boy	14 (37.84)
Race, n (%)	Asian	37 (100)
Age (months)	Mean (SD)	17.75 (11.11)
Height (cm)	Mean (SD)	73.18 (13.90)
Weight (kg)	Mean (SD)	8.83 (2.53)

Efficacy Parameters

TNSS Score

The mean TNSS reduced from 1.30 at baseline to 0.55 within 10 minutes (p<0.0001) and 0.26 at 30 minutes (p<0.0001). Further reductions were observed at 1 hour (0.15; p<0.0001) and 2 hours (0.05; p<0.0001). By 3 hours, the mean of TNSS reached 0.00 (p<0.0001). On Day 7, the mean TNSS remained low at 0.05, with reported minimal recurrence (Figure 1).



***p value is <0.05 is considered clinically significant**

Figure 1: Change in total Nasal Symptom Scale (TNSS) over time (N=37)

VAS Score

The VAS score showed 62.16% participants experienced relief in symptoms within 2 minutes, which increased to 94.59% by 5 minutes and 100% by 8 minutes. On average, the onset of relief was observed within 4 minutes. (Figure 2a)

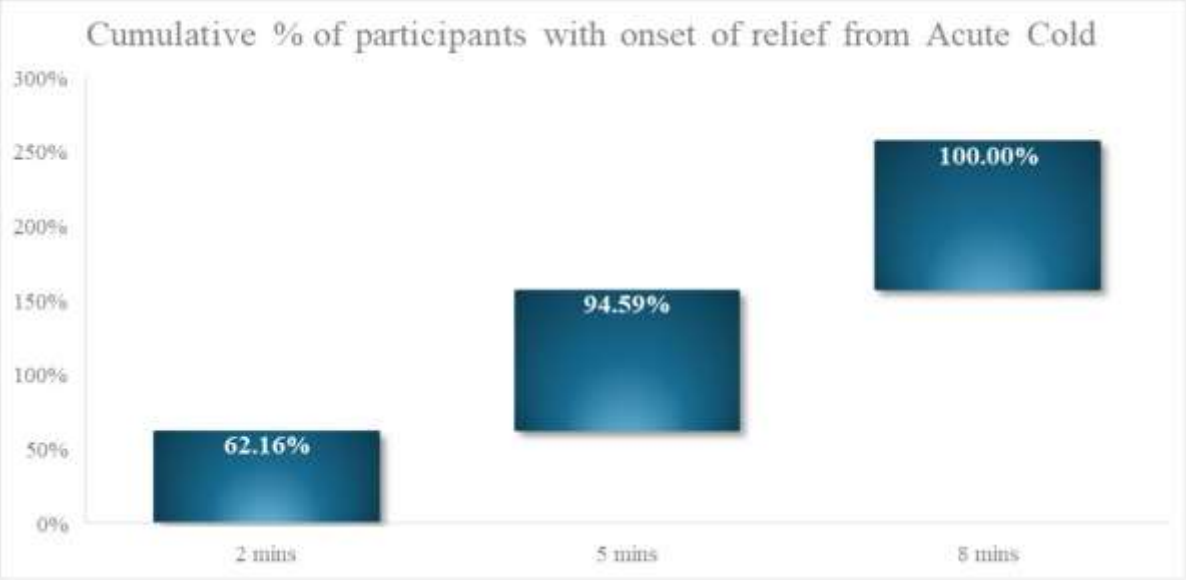


Figure 2a: Onset of relief from acute cold symptoms (N=37)

Overall relief was achieved in 21 participants (56.8%) within 13 minutes and in 30 participants (81.1%) within 30 minutes. Relief was reported in 34 participants (91.9%) by 2 hours 15 minutes, and by 3 hours all participants had experienced overall relief. The mean time to overall relief was 32 minutes. All participants achieved overall relief of cold symptoms within 3 hours, with a mean time to relief of approximately 30 minutes. (Figure 2b)

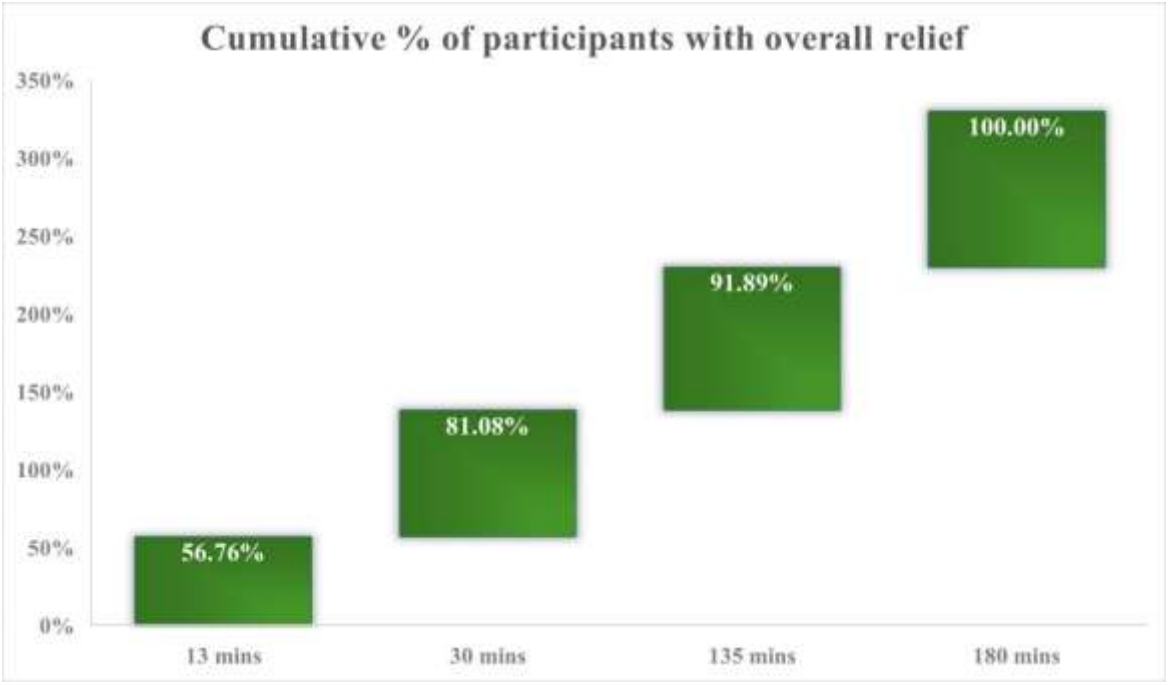


Figure 2b: Overall cold relief from acute cold symptoms (N = 37)

Tissue Absorbent Test

The results showed that 94.59% of participants were graded as 1, and remaining 5.41% were grade 2. None of the participants were graded in 3, 4, or 5.

Subjective Perception Questionnaire

At the end of study, 100% of caregivers reported that participants experienced a sensation of nasal cooling and that the investigation product was gentle and mild on the skin. Additionally, all caregivers agreed that the investigation product calmed, soothed, and relaxed participants from the first use and began easing discomfort immediately. Regarding sleep outcomes, 100% of caregivers reported that participants experienced restful, peaceful, all-night sleep, with 59% of participants achieving undisturbed sleep for up to 10 hours after 7 days of use.

The investigation product was reported to be non-greasy, non-sticky, and non-staining with its aroma as optimum and effective in relieving nasal discomfort by all caregivers. Overall, 100% of caregivers expressed satisfaction with the investigation product after 7 days. (Table 2)

Table 2. Caregiver-reported outcomes following 7 days of use (N = 37)

Parameter Evaluated	Caregivers reporting "Yes"	Percentage (%)
Cooling effect observed	37	100%
Gentle and mild on baby's skin		
Calms, soothes, and relaxes baby		
Relief from discomfort from first use		
Improved breathing		
Participants experienced restful, all-night sleep		
Caregivers experienced restful sleep		
Participants had peaceful sleep for 10 hrs		
Participants had peaceful sleep for 8 hrs		
Caregivers had peaceful sleep for 8 hrs		
Caregivers had peaceful sleep for 10 hrs		
Non-sticky, non-greasy, non-staining		
Aroma optimum and effective for relieving discomfort		
Overall satisfaction with product		

Safety Parameters

None of the participants experienced any adverse events such as redness, dryness, itchiness, burning sensation.

DISCUSSION

In this trial, we evaluated the investigation product containing natural essential oils (eucalyptus, peppermint, and rosemary in a coconut oil base) for relief of acute cold symptoms in infants aged 0–36 months. The results showed that the investigation product produced a prompt and significant reduction in participants nasal symptom scores as early as the first 10–30 minutes. Additionally, Caregivers in our study reported that participants were calmer, slept more peacefully, and had easier breathing after investigation product use, which accords with literature describing how aromatic treatments can reduce nocturnal discomfort and improve sleep in children with colds.[20] Improved infant sleep and relief from irritability likely benefitted the caregivers' own rest – indeed, prior studies have observed that when children's cold symptoms are relieved with aromatics, parental sleep quality also significantly improves.[3]

The rapid onset of relief observed in our study is biologically plausible: menthol from peppermint oil and 1,8-cineole (eucalyptol) from eucalyptus oil are known to stimulate cold-sensitive trigeminal receptors (TRPM8) in the nasal mucosa. [15,16] This neurophysiological mechanism creates a sensation of easier breathing even without measurable changes in airway resistance. [17,18] Such a sensory mode of action can explain the immediate comfort and

decongestion reported, consistent with other studies noting that aromatics improve subjective congestion and wellness despite minimal objective change in airflow.[19] A randomized trial in children reported that a vapor rubs with similar essential oils led to greater night-time symptom improvement than placebo, with the most pronounced benefits seen in sleep quality for both the child and the parents.[14] This suggests that aromatic ointments can meaningfully improve subjective nasal congestion in similar ailments.

The natural constituents of investigation product have properties that probably act in synergy. Eucalyptus oil (rich in 1,8-cineole) possesses antiviral, antibacterial, and anti-inflammatory activities, and has traditionally been used to combat respiratory congestion while promoting relaxation and calmness. Peppermint oil provides menthol, a cooling decongestant that can soothe the airways and help relax the child. Rosemary oil contributes additional anti-inflammatory effects, potentially reducing local swelling. Notably, 1,8-cineole has been shown to modulate airway inflammation by downregulating NF-κB–mediated cytokine production (e.g. inhibiting TNF-α and IL-1β), and it can even decrease mucus hypersecretion by suppressing mucin gene expression in respiratory epithelium. [22,23] These suggests that beyond symptomatic sensory relief, the essential oils might impart a mild direct benefit on the underlying inflammation and secretions in a cold. Moreover, the inclusion of coconut oil as the base ensures a non-irritant formulation that is quickly absorbed into the skin, enhancing suitability for delicate skin and caregiver acceptability.

Overall, our study indicates that the investigation product is a safe and effective remedy for infants and toddlers with common cold symptoms, providing prompt relief and improving the child's comfort and ability to sleep. This has practical implications for real-world pediatric care, as it offers caregivers a viable option during the infancy/toddler period when conventional decongestants and cough medicines are neither recommended nor available. By alleviating participants congestion and distress, such interventions can improve quality of life for both participants and caregivers.

The study had several limitations such as this was an open-label study and lacked a placebo arm, which may have introduced caregiver bias. Safe use of aromatic oils in infants and toddlers also requires careful application to the chest or back, avoiding the face and nostrils.[24] Reliance on caregiver-reported outcomes in an unblinded setting further increases susceptibility to expectation effects. The small sample size limits statistical power, generalizability, and the ability to draw firm safety conclusions in this sensitive age group.

CONCLUSION

The present study demonstrates that the investigation product is a safe, well-tolerated, and effective topical option for infants and toddlers with acute cold symptoms. The formulation was well tolerated with no adverse events, improved sleep and calming effects, and achieved high caregiver satisfaction, supporting its role as a safe, non-pharmacological alternative for managing acute colds in early childhood.

Declaration by Authors

Ethical Approval: Approved

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