Evaluation of efficacy and safety of Acne-N-Pimple cream in acne vulgaris

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Abstract
Acne vulgaris is a common skin disorder and the available drugs have been shown to be associated with specific limitations. The present study was planned to evaluate the efficacy and safety of “Acne-N-Pimple Cream” in the management of acne vulgaris.

This study was a prospective, open, non-comparative, phase III clinical trial and a total of 26 patients, who were diagnosed as suffering from acne vulgaris were included in the study. Children below 18 years of age, patients with pre-existing systemic disease necessitating long-term medication, genetic and endocrinal disorders, and those who refused to give informed consent were excluded from the study. Pregnant or lactating women were also excluded from the study. A baseline history was obtained, which included personal data, a description of symptoms and details of past medical history and thereafter all patients underwent a clinical examination and thorough skin examination. All the patients were advised to apply the “Acne-N-Pimple Cream” on the affected area, twice daily for a period of 6 weeks. All the patients were followed up for a period of 6 weeks. The predefined primary efficacy endpoints were reduction in number of blackheads and whiteheads, inflamed pustules and overall inflammation along with an increase in exfoliation, overall moisturizing and soothing effect, and healing without scar formation. The predefined secondary safety endpoints were incidence of adverse events and compliance to the drug treatment.

This study observed significant reduction in the number of blackheads and whiteheads, in number of inflamed pustules and overall inflammation. Similarly there was enhanced exfoliation, moisturizing and soothing effect along-with significant improvement in healing without scar formation. There were no clinically significant short- and long-term adverse reactions, during the entire period of the study and excellent patient compliance to “Acne-N-Pimple Cream” was observed. The excellent results obtained might be due to the antioxidant, anti-inflammatory, antiandrogenic and antimicrobial properties of the ingredients. Therefore, it may be concluded that “Acne-N-Pimple Cream” is clinically effective and safe in the management of acne vulgaris.

Introduction
Acne vulgaris is a common skin disorder, affecting virtually all adolescents and adults at some time in their lives. Although the overall health is not impaired, acne is not a trivial disease, as it can produce cutaneous and emotional scars that last a lifetime.¹⁻³ Numerous psychological problems stem from acne, some even resulting in decreased employability in adulthood.⁴

The etiology of acne is multifactorial and according to the severity of inflammation, acne is classified into purely comedonal (non-inflammatory acne), mildly papular, scarring papular and scarring nodular acne. Clinically, the peak incidence of acne is evident during the teen
years, but a significant chunk of men and women between 20–40 years of age also suffer from acne vulgaris.\textsuperscript{5,6}

Topical therapy is recommended for the management of acne vulgaris, especially for patients with non-inflammatory comedones and mild to moderate inflammatory acne. Comedolytic and anti-inflammatory agents along with antimicrobials are generally preferred in topical treatment of acne. But, the available drugs used for topical and systemic management of acne, have been shown to be associated with specific limitations. For example, topical application of tretinoin leads to dermal adverse reactions (erythema, peeling and burning of the skin). During the past few decades many reports have documented an emergence of antibiotic resistance by \textit{Propionibacterium acnes} during the treatment of acne\textsuperscript{7-9} and systemic antimicrobials have been causally associated with various short- and long-term adverse effects).\textsuperscript{10}

“Acne-N-Pimple Cream” is a polyherbal formulation recommended for the management of acne vulgaris and it contains the powders of \textit{Lenus culinaris} and Alum, with extracts of \textit{Salmalia malabarica}, \textit{Vitex negundo} and \textit{Aloe barbadensis}. The present study was planned to evaluate the efficacy and safety of “Acne-N-Pimple Cream” in the management of acne vulgaris.

\textbf{Study aim}

This study was planned to evaluate the clinical efficacy and safety (short- and long-term) of “Acne-N-Pimple Cream” in the management of acne vulgaris.

\textbf{Study design}

This study was a prospective, open, non-comparative, phase III clinical trial, conducted at the department of Dermatology of The Apollo Hospitals, Chennai, India, as per the ethical guidelines of Declaration of Helsinki, from June to September 2004. The study protocol, case report forms, regulatory clearance documents, product related information and informed consent form (in Tamil and English) were submitted to the “Institutional Ethics Committee” and were approved by the same.

\textbf{Materials and methods}

\textbf{Inclusion criteria}

A total of 26 patients, who were diagnosed as suffering from Acne vulgaris, and who were willing to give informed consent were included in the study.

\textbf{Exclusion criteria}

Children below eighteen years of age, patients with preexisting systemic disease necessitating long-term medication, genetic and endocrinal disorders, and those who refused to give informed consent were excluded from the study. Pregnant the lactating women were also excluded from the study.

\textbf{Study procedure}

A baseline history was obtained in order to determine the patient’s eligibility for enrolment in the trial. The baseline assessment included personal data, a description of symptoms and details of past medical history (family history of acne, history of possible exacerbating factor/s, etc.). Thereafter, all the patients underwent a clinical examination and thorough skin examination was done for presence of black and white heads, inflamed papules and pustules,
and cysts and nodules. All the patients were advised to apply the “Acne-N-Pimple Cream” on the affected area, twice daily for a period of 6 weeks.

**Follow-up and monitoring**
All the patients were followed up for a period of 6 weeks and at each weekly follow-up visit, the improvement in the acne lesions was evaluated. At the end of the 6th week, the overall performance of the “Acne-N-Pimple Cream” was evaluated.

**Primary and secondary endpoints**
The predefined primary outcome measures were reduction in the number of blackheads and whiteheads, inflamed pustules and overall inflammation along with an increase in exfoliation, overall moisturizing and soothing effect and healing without scar formation. The predefined secondary outcome measures were incidence of adverse events and compliance to the drug treatment.

**Adverse events**
All local and systemic adverse events, reported or observed by patients were recorded along with information about severity, time of onset, duration and action taken regarding the study drug. Relation of adverse events to study medication was predefined as “Unrelated” (a reaction that does not follow a reasonable temporal sequence from the time of administration of the drug), “Possible” (follows a known response pattern to the suspected drug, but could have been produced by the patient’s clinical state or other modes of therapy administered to the patient), and “Probable” (follows a known response pattern to the suspected drug that could not be reasonably explained by the known characteristics of the patient’s clinical state).

Patients were allowed to voluntarily withdraw from the study, if they had experienced serious discomfort during the study or sustained serious clinical events requiring specific treatment. For patients withdrawing from the study, efforts were made to ascertain the reason for dropout. Non-compliance (defined as failure to take less than 80% of the medication) was not regarded as treatment failure, and reasons for non-compliance were noted.

**Results**
A total of 26 patients were included in this study and the age range was 20-30 years. There was a significant reduction in number of blackheads and whiteheads, from 2nd week onwards, when compared to the baseline. There was significant reduction in number of inflamed pustules, when compared to the baseline and the overall inflammation, as judged clinically was also significantly improved when compared to the baseline. Similarly, exfoliation also showed significant improvement when compared to the baseline.

![Figure 1: Response to drug treatment (Acne-N-Pimple cream)](image-url)
There was enhanced moisturizing effect from the 2nd week onwards and in addition, the soothing effect was also improved when compared to the baseline. There was a significant improvement in healing without scar formation.

The overall response to the drug treatment also recorded a significant improvement from the 2nd week onwards and 14 (54%) patients graded the treatment as good, 10 (38%) patients graded the treatment as very good, while 1 subject (4%) graded the treatment as excellent (Figure 1).

There were no clinically significant short- and long-term adverse reactions (either reported by the patients or observed by the investigators), during the entire period of the study and excellent patient compliance to “Acne-N-Pimple Cream” was observed.

**Discussion**

Acne vulgaris is a chronic inflammatory disease of the pilosebaceous units. The etiologic factors include increased sebum production, ductal hyperkeratosis, abnormality of the microbial flora within the pilosebaceous unit, and chemomediators of inflammation. The dermal inflammation is not due to presence of bacteria, but from biologically active chemomediators produced by *P. acnes* and the microenvironment within the pilosebaceous unit, is probably more important than the absolute number of *P. acnes* organisms. Indeed, the major role of the sebaceous gland appears to be supplying nutrients needed by *P. acnes* and moreover, the microbiologic principle of biofilms appears to be applicable to *P. acnes* in acne.11

The recent demonstration that the ‘peroxisome proliferator activated receptors’ (whose natural ligands are polyunsaturated fatty acids and theirs oxidation products), have a central role in the induction of acne, has indicated new links between free radicals and skin inflammation.12 Further, it has been shown that androgens also play an important role in the pathogenesis of acne through the stimulation of sebum secretion, increasing sebaceous gland size and possibly through follicular hyperkeratinization.13

Acne is associated with a greater psychological burden than a variety of other disparate chronic disorders. Various studies have demonstrated that patients with acne vulgaris suffer psychological aberrations like depression, anxiety, psychosomatic symptoms (pain and discomfort), embarrassment and social phobia. Effective treatment of acne vulgaris is accompanied by improvements in self-esteem, social assertiveness and self-confidence.14

This study observed significant reduction in the number of blackheads and whiteheads, in the number of inflamed pustules and overall inflammation. Similarly, there was enhanced exfoliation, moisturizing and soothing effect along with significant improvement in healing without scar formation. These positive benefits seen in this study might be due to the synergistic action of the constituents of “Acne-N-Pimple Cream”.

*Lenus culinaris* is rich in polyphenols and the major monomeric flavans are catechin-3-glucose, with lesser amounts of catechin and epicatechin.15 Alum (aluminium sulphate) acts as potent stringent and antiseptic, which is beneficial in acne vulgaris.

The antioxidant properties of *Aloe barbadensis* have been well documented.16 Hu et al. demonstrated the antioxidant activity of polysaccharide and flavonoid concentrations of *Aloe*...
barbadensis and found that the antioxidant activity was higher than that observed with alphatocopherol.\textsuperscript{17} Caffeoyl aloesin is a powerful antioxidant compound isolated from Aloe barbadensis, which has antiinflammatory and antioxidant activities. Aloesin has been shown to inhibit tyrosine hydroxylase and dihydroxyphenylalanine (DOPA) oxidase activities of tyrosinase from normal human melanocyte cell lysates.\textsuperscript{18} Bautista et al. demonstrated the antiinflammatory activity of Aloe barbadensis and documented the inhibition of bradykinin activity.\textsuperscript{19}

Vitex negundo has astringent, anti-inflammatory, analgesic (possibly mediated via prostaglandin synthesis inhibition), antihistaminic, membrane stabilizing and antioxidant activities.\textsuperscript{20} In one study, the flavonoid-rich fraction (5,7,3'-trihydroxy, 6,8,4'-trimethoxy flavones) of Vitex negundo was found to antagonize the androgenic action of exogenous testosterone propionate.\textsuperscript{21} Rani et al. documented the antibacterial and antifungal properties of Salmalia malabarica, which are attributed to ‘shamimin’ a flavonol C-glycoside.\textsuperscript{22,23}

Andrographis paniculata has immunomodulatory and antimicrobial effects, and the antimicrobial activity is due to the synergistic effect of the arabinogalactan proteins and andrographolides.\textsuperscript{24}

Conclusion
Acne vulgaris is a common skin disorder, affecting virtually all adolescents and adults at some time in their lives. Although the overall health is not impaired, acne is not a trivial disease, as it can produce cutaneous and emotional scars that last a lifetime. The present study was planned to evaluate the efficacy and safety of “Acne-N-Pimple Cream” in the management of acne vulgaris.

This study observed significant reduction in number of blackheads and whiteheads, in number of inflamed pustules and overall inflammation. Similarly, there was enhanced exfoliation, moisturizing and soothing effect along with significant improvement in healing without scar formation. There were no clinically significant short- and long-term adverse reactions, during the entire period of the study and excellent patient compliance to “Acne-N-Pimple Cream” was observed.

The excellent results obtained might be due to the antioxidant, anti-inflammatory, antiandrogenic and antimicrobial properties of the ingredients of “Acne-N-Pimple Cream”. Therefore, it may be concluded that “Acne-N-Pimple Cream” is clinically effective and safe in the management of acne vulgaris.

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References