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# Evaluation of Efficacy and Safety of Perfact Face Gel and Perfact Face Tablets in Management of Acne

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## Abstract

Acne is a common disease of the pilosebaceous units of the skin and topical therapy is recommended for the management of acne with comedolytic, anti-inflammatory agents, along with antimicrobials. However, topical application of these drugs leads to frequent adverse effects and also, there is an emergence of antibiotic resistance by Propionibacterium acnes. Furthermore, systemic antimicrobial usage has been causally associated with various adverse events. No simple recipe for the treatment can be provided. Treatment options vary with the stage and severity of the disease. So now a day's physicians prefer the herboformulations containing *Melaleuca alternifoli*, *Azadirachta indica, Curcuma longa*, *Piper nigrum, Aloe vera, Citrus bergamia, Santalum album, Rosa centifolia, Carica papaya* etc. than the allopathic drugs due to less or no side effects. Perfact gel is herbal formulation contains 5% of *Melaleuca alternifoli* (Tea tree oil) and Perfact tablet is polyherbal formulations and contains extracts of *Azadirachta indica, Curcuma longa*, and *Piper nigrum,* and the study was conducted to evaluate the efficacy and safety of perfect face, Perfect face tablets and both in the management of acne.

In this contest, the present work is carried out which includes Uncontrolled randomized, open labelled, multicentric Phase III clinical trial using oral Ayurvedic multicomponent preparations with or without use of Ayurvedic dermatological formulation in three different hospitals from 15 July 2009 to 15 Oct 2009. One hundred fifty three patients (n=153) including 63 males and 90 females in the age group of 35-50 years were enrolled. Children below 18 years of age, patients with preexisting systemic disease necessitating long-term medications, genetic and endocrinal disorders and those who refused to give informed consent were excluded from the study. Pregnant and lactating women were also excluded from the study. A baseline history was obtained in order to determine the patient's eligibility for enrolment in the trial. Thereafter all patients underwent a clinical examination and thorough skin examination was done the subjects are divided in to three groups. Group I received Perfect oral Tablet, Group II received dermatological gel (Perfact Face gel) and Group III received oral tablet and dermatological gel formula. Efficacy was assessed by the ability of perfact face gel and perfact face tablets to reduce the number of inflamed and non-inflamed lesions by using Leed's counting method and Cardiff index method. The group III shows more 12% as compared to group II. It was concluded that group III having more significant effect on the inflamed lesion as compared to group I and II treatment.

**Keywords:** Acne; Herbal; Clinical trial

## Introduction

Acne vulgaris, a chronic inflammatory disorder in adolescents consists of the pilosebaceous follicles, characterized by comedones, papules, pustules, cysts, nodules and often scars, chiefly on face, neck etc [1]. It is a skin condition that occurs due to the clogging of oil glands of the skin [2]. The oil that normally lubricates the skin gets trapped in blocked oil ducts and results in what we know as Pimples (a small skin swellings that sometimes contain pus), Blackheads (a dark formations on the skin due to an accumulated mixture of oil and cells in a blocked skin pore) and Whiteheads (a small flesh-or white-colored bumps due to skin pore blockage on the surface of skin). Sometimes it also includes deeper skin lesions that are called C**ysts** (a closed sac beneath the skin or deeper that contain fluid or semisolid substances) [ 3] It is more common during teenage years but is known to happen across all age. Adult acne is becoming increasingly popular [4]. It is a disease of the skin which can be painful for those suffering from moderate to severe acne [5]. Acne vulgaris mostly affects the areas of skin with the densest population of sebaceous follicles [6] these areas include the face, the upper part of the chest, and the back. The cause of acne is unknown. It is presumed to be activated by androgens in genetically predisposed individuals [7]. The earliest abnormalities in acne are:

- Increased sebum production due to which the skin looks greasy (seborrhea)
- Formation of horny plugs (comedones)

The general therapy in the treatment of acne vulgaris includes oral and topical therapy employing comedolytics (Benzoyl peroxide, Tretinoin, Azeleic acid and Isotretinoin) and antibiotics for both oral and topical use (Tetracycline, Erythromycin, etc.) [8]. In addition to producing bacterial resistance [9], these drugs have several side effects. These are described for Tetracycline, Erythromycin [10], Clindamycin [11] and Isotretinoin [12]. Although natural products are safer than necessarily synthetic antibiotics, some patient prefer to use herbal medicine [13]. So now a day's physicians prefer the herb formulations containing *Melaleuca alternifoli*, *Azadirachta indica, Curcuma longa*, *Piper nigrum, Aloe vera, Citrus bergamia, Santalum album, Rosa centifolia, Carica papaya* etc [14] than the allopathic drugs due to less or no side effects.

Many hundred of plants worldwide are used in traditional

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medicine as treatment for Acne. Some of these have been subjected to *invitro* screening but efficacy of such herbal medicine has seldom been rigorously tested in clinical trials [15]. It is surprising that so few clinical trials have tested the efficacy of herbal antibiotics.

However, claims have not been supported with uncontrolled clinical trials.

The work reported here includes uncontrolled Phase iii clinical trials conducted using oral multicomponent Ayurvedic preparation with or without the use of ayurvedic dermatological formulation developed in the company.

## Material and Method

### Materials

Perfact face gel-It contains 5% tea tree (Melaleuca alternifolia oil) and manufactured by Panacea Biotec Ltd Larlu, Punjab India.

Perfact face tablet- It contains Neem extract 200 mg, Turmeric extract 200 mg and Piper extract 10 mg are manufactured by Panacea Biotec Ltd Larlu, Punjab India.

### Study design

This study was an open, Randomized, uncontrolled Phase III clinical trial conducted at three centres, B.M Hospital Ghaziabad, Sumitra Hospital Noida and Clinic-441 Gurgaon, as per the ethical guidelines of the Declaration of Helsinki and Good Clinical Practices (ICH E6). The study protocol, case report forms (CRFs), regulatory clearance documents, product-related information and informed consent forms (English and Hindi) were submitted to the Institutional Ethics Committee and approved by the same.

### Patients

The study was conducted in 153 patients, 63 males and 90 females.

**Inclusion Criteria:** One hundred and fifty three patients of both sexes in the age group of $\geq$15 to $\leq$ 50, of the out-patient from three hospitals were included in the study. A written informed consent was obtained from all patients.

**Exclusion criteria**: The patients excluded in the studies were pregnant women, breast feeding mothers and those patients who had previous history of hypersensitivity to ayurvedic drugs, serious hepatic or renal insufficiencies and those on treatment with other antibiotics corticosteroids, retinoid, anticonvulsants and androgens in the preceding four weeks. Patients excluded in the study were taking any hormonal preparations e.g. oral contraceptive pills. Individuals participating in new drug evaluation programme in proceeding 3 months. Patients with apparent physical or mental abnormalities. Patients who have not taken any anti acne medication for last three months.

### Clinical studies

Following good clinical practices guideline, a randomized, open label, multicentre study was conducted in three centers (Ghaziabad, Noida and Gurgaon). One hundred fifty three patients (n=153) including 63 males and 90 females in the age group of 35-50 years were enrolled. They had mild to moderately acne exhibiting a minimum of 10 inflammatory lesions.i.e papules and pustules and minimum of five non inflammatory lesions i.e. blackheads.

### Examination

The patients were examined for the following parameters before being included in the trial. (1) Height (2) bodyweight (3) blood pressure (4) body status (5) LFT (6) KFT (7) Hematogrm. Each patient history was recorded for their (1) gastrointestinal motility (2) eating habits (veg/non veg), (3) previous history of illness, (4) Seasonal occurrence acne syndrome (5) effect of previous therapy and other relevant details.

Written informed consent was obtained from the patients after explaining to them the purpose of conducting the trial. They were randomized into three groups with 48,46and 47 patients in group I, II and III respectively. They were suitably randomized. Out of total number of patient, 10 patients dropped out of trial from respective group.

Group I received oral tablets (Perfact Tablet) containg active ingredients.

Group II received dermatological gel (Perfact gel) preparation containg active ingredients.

Group III received oral tablets containg active ingredients with dermatological gel formulation containing active ingredients.

## Dosage and Care Regimen

After completing the clinical examination, each patients in group I, II and III was given in the packet with 14 tablets containing active ingriedents.Sufficient amount of topical preparation to last at least for a week was given in the collapsible tube to each patient in group II and III .They were explained in their local language to take one tablet twice a day and to apply the topical preparation once daily on the effected area. Total duration of study treatment was 4 weeks. The patient was directed not to take any other medication and not to use any antimicrobial agent containing soap or any cosmetics during the trial without investigator's permission. They were asked to report to the clinic every 7$^{th}$ day for a weeks. During each visit, front and bilateral 45° side facial views of every patient were taken using a 5 megapixel 35 mm digital camera system. After the each visit a colour picture of face was taken for counting the lesion. For taking the photographs special instructions were followed by investigator. After counting the lesions, scoring was given according to Leed's counting Technique.

| Age | No. of Patients |
|---|---|
| <30 Yrs | 139 |
| 30-50 Yrs | 13 |

Age Missing: Pt. ID- N39

**Table 1:** Demographic data of all the subjects participating in clinical trial.

| Time Interval | No. of Patients |
|---|---|
| <3 Months | 21 |
| 3 to 6 Months | 59 |
| 6 months to 1 Yr | 53 |
| 1 to 3 Yrs | 16 |
| > 3 Yrs | 2 |

**Table 2:** Presence of Acne with Time.

| Type of lesion(Tablet) | | Week 0 | Week 2 | Week 4 | P value |
|---|---|---|---|---|---|
| Non Inflamed | Whiteheads | 11.146 | 6.292 | 3.396 | 0.01460 |
| | Blackheads | 10.167 | 5.333 | 0.961 | 0.00021 |
| Inflamed | Papules | 10.167 | 5.063 | 2.729 | 0.00000 |
| | Pustules | 4.125 | 1.375 | 0.563 | 0.00001 |
| Deep | Nodules | 2.542 | 1.979 | 1.729 | 0.45747 |
| | Cysts | 1.750 | 1.375 | 1.396 | 0.53849 |

**Table 3:** Showing the change in total no .of lesions with treatment with perfact tablets.

| TYPE OF LESION(GEL) | | WEEK 0 | WEEK 2 | WEEK 4 | P VALUE |
|---|---|---|---|---|---|
| Non Inflamed | Whiteheads | 10.24 | 6.20 | 3.37 | 0.00881 |
| | Blackheads | 10.11 | 5.24 | 2.80 | 0.00086 |
| Inflamed | Papules | 11.67 | 6.67 | 3.33 | 0.00000 |
| | Pustules | 3.02 | 1.76 | 1.41 | 0.00765 |
| Deep | Nodules | 1.20 | 1.04 | 1.07 | 0.71785 |
| | Cysts | 1.24 | 1.17 | 1.13 | 0.79429 |

**Table 4:** Showing the change in total no. of lesions with treatment with perfact gel.

| TYPE LESION (GEL+TABLET) | | WEEK 0 | WEEK 2 | WEEK 4 | PVALUE |
|---|---|---|---|---|---|
| Non Inflamed | Whiteheads | 9.917 | 5.313 | 2.208 | 0.00001 |
| | Blackheads | 11.292 | 6.250 | 2.104 | 0.00009 |
| Inflamed | Papules | 14.292 | 6.604 | 3.058 | 0.00000 |
| | Pustules | 4.229 | 1.958 | 0.729 | 0.00000 |
| Deep | Nodules | 2.875 | 2.042 | 1.688 | 0.2763 |
| | Cysts | 2.567 | 2.104 | 2.104 | 0.943 |

**Table 5:** Showing the change in total no. of lesions with treatment with perfact gel & perfact tablets.

| Treatment Group | No. of weeks | N | CAD[a] Score |
|---|---|---|---|
| I | Week 0 | 48 | 8.45±0.48 |
| | Week 4 | 48 | 4.97±0.49 |
| II | Week 0 | 46 | 8.45±0.46* |
| | Week 4 | 46 | 4.82±0.24* |
| III | Week 0 | 47 | 8.56±0.47 |
| | Week 4 | 47 | 4.78±0.48 |

[a]**Cardiff acne disability, Values are presented as Mean±S.E.**M. Paired t- test, significant at *p<0.01.

**Table 6:** Cardiff Acne disability score for all Treatment Groups.

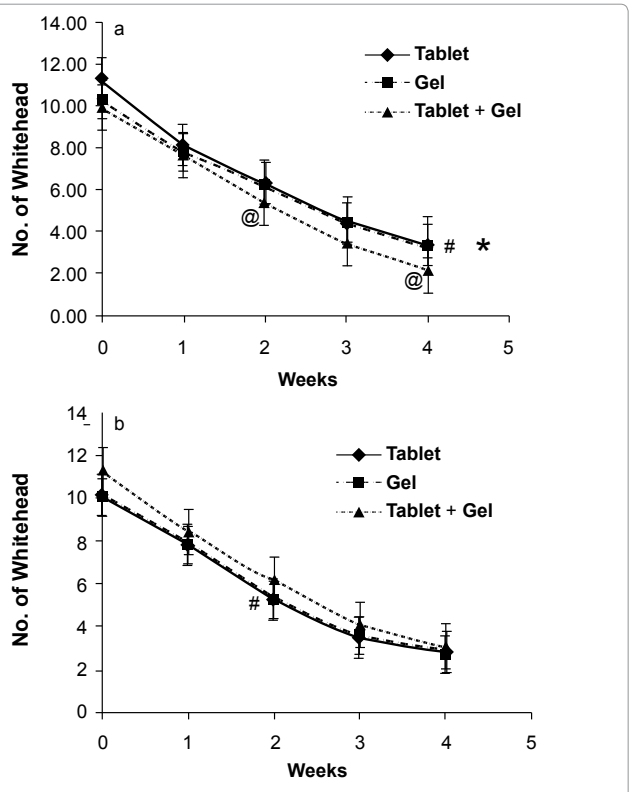


**Figure 1:** Change in no. of noninflamed lesions with time with all treatment groups (a) whiteheads (b) blackheads (n=48) *P<0.05 tablet, # P<0.05 gel, @ P<0.05 tablet+gel.

## Clinical evaluation

A single physician recorded all the clinical observations using assessment scale ((Leeds count [16] and Cardiff Acne disability Index [17]).In this patient overall change in facial acne compared with his or her appearance at the beginning of study was made on the four point scale ranging from excellent to poor response. The first overall assessment of the acne severity in a particular area (grade between 0 to10) is accurate, reproducible, rapid and suitable for use in routine clinic.

Statistical analysis was done using paired t-test and Pearson's coefficient of correlation. Mean values (+/- standard deviation) will be calculated, as well as variations of the parameters relative to pre treatment values (expressed in %). Two-tailed paired Student's t test will be used to determine the significance of the results (comparisons between pre-treatment, after 2 weeks and after 4 weeks of treatment) for the parameters determined with the level of significance being set at 5%.The minimum level of significance was fixed at 95% confidence limit and a 2-sided p value of <0.05 was considered significant. The values are expressed in the sequence as: mean score (M) at 2nd and 4th week, standard deviation (SD) at baseline, 2nd and 4th week, standard error of mean (SEM) at 2nd and 4th week lower 95% confidence interval (CI) of mean at 2nd and 4th week, upper 95% confidence interval (CI) of mean at 2nd and 4th week, squared R value, p value, significant (S). In all graphs, the baseline value is 0.00.

## Results

Demographic distribution of patient included in the study is shown in Table 1 and 2.In all 141 patients completed the study and there were twelve dropouts. None of patients were non-compliant with respect to drug administration and application. Total non inflamed lesions i.e.

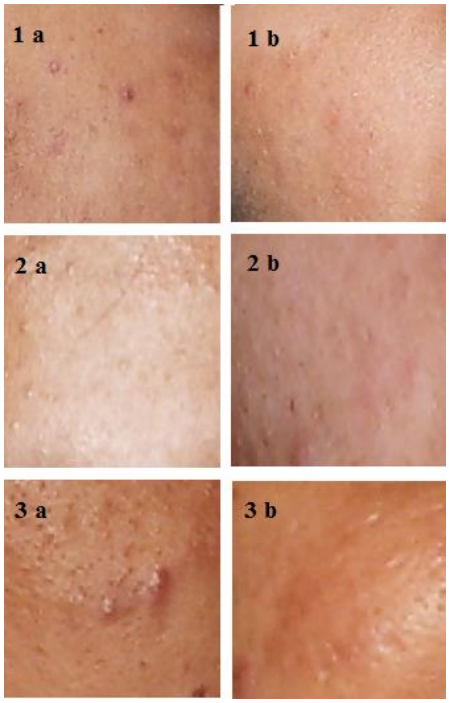


**Figure 2:** Shows the Presence of whiteheds before the treatment and after the treatment in all the treatment group.(1.a) Group I before treatment (1.b) Group II after treatment, (2.a) Group II before treatment (2.b) Group II after treatment,(3.a)Group III before treatment (3.b)Group III after treatment.

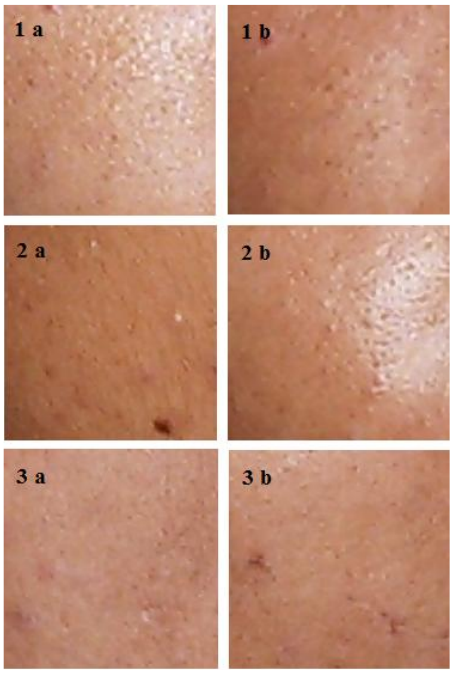


**Figure 3:** Shows the Presence of Blackheads before the treatment and after the treatment in all the treatment group.(1.a) Group I before treatment (1.b) Group II after treatment, (2.a) Group II before treatment (2.b) Group II after treatment,(3.a)Group III before treatment (3.b)Group III after treatment.

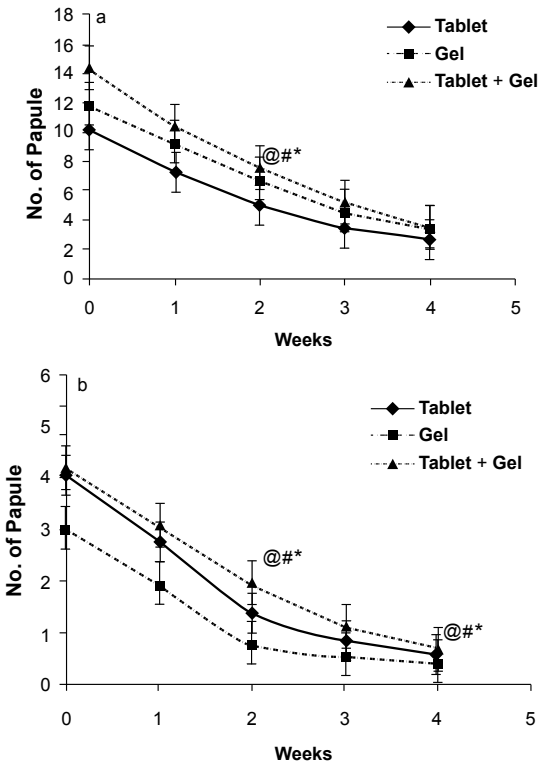


**Figure 4:** Change in no. of inflamed lesions with time with all treatment groups (a) Papules (b) Pustules (n=48) * P<0.05 tablet, # P<0.05 gel, @P<0.05 tablet+gel.

total number of white heads and black heads gradually reduced during the treatment and the reduction was statistically significant at 2nd and 4th week of therapy as compared to total non inflamed lesions on the day of screening of subjects.

A decrease in total number of white heads in the subjects was observed that was statistically significant at week 2 and week 4 when compared to the white heads at week 0. (Figure 1a), (Figure 2) Table 3 showing the change in total no .of lesions with treatment with perfact tablets.

The percentage improvement in blackheads was found to be similar in all the groups. Group I shows the improvement from 47.5% at week 2 to 74.11% at week 4. Group II shows the improvement from 48.17 % at week 2 to 78.3% at week 4.In case of Group III, similar improvement was observed. The difference at week 2 and 4 was found to be statistically significant when compared to mean number of blackheads at the start of therapy (Figure b),(Figure 3) The improvement of Papules was 73.22%, 71.4% and 75.8% at week 4 in Group I, II, and III respectively (Figure 4a),(Figure 5). The Group II shows less improvement as compare to other group. The difference at week 2 and week 4 was found to be significant when compared to mean number of inflamed lesion at the start of therapy. The improvement of Pustules was 86.35.0%, 86.40% and 82.70% at week 4 in Group I, II, and III respectively (Figure 4b),(Figure 6). It is observed that Cyst showed improvement of 2.2%, 8.8% and 2.9% after 4 weeks of treatment in Group I, II and III respectively (Fig. No.7.a).The improvement of nodules was 31.9%, 13.00% and 41.2% at week 4 in Group I, II, and III respectively (Figure 7b),(Figure 8). There was no serious adverse event reported during the entire course of study.

## Discussion

As per the guidelines of The American Academy of Dermatology, primary acne vulgaris is classified into mild, moderate and severe grades.

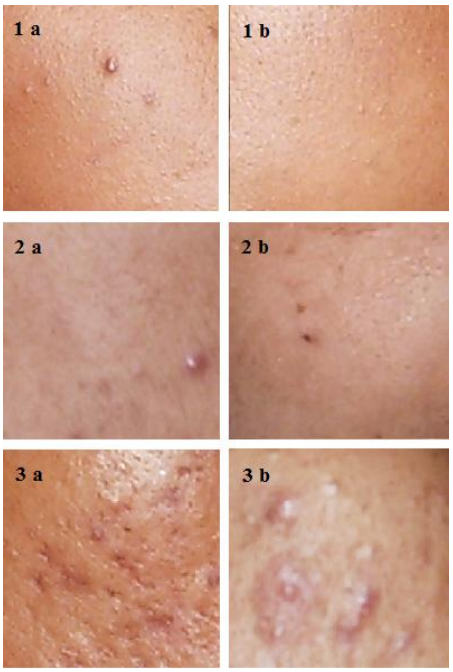


**Figure 5:** Shows the Presence of Papules before the treatment and after the treatment in all the treatment group.(1.a) Group I before treatment (1.b) Group II after treatment, (2.a) Group II before treatment (2.b) Group II after treatment,(3.a)Group III before treatment (3.b)Group III after treatment.

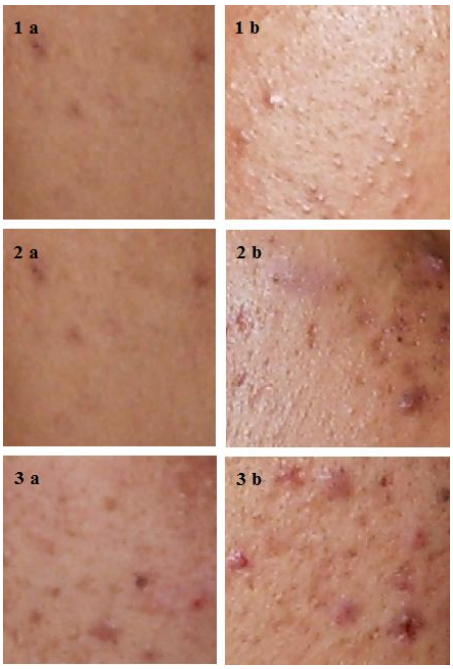


**Figure 6:** Shows the Presence of Pustules before the treatment and after the treatment in all the treatment group.(1.a) Group I before treatment (1.b) Group II after treatment, (2.a) Group II before treatment (2.b) Group II after treatment,(3.a)Group III before treatment (3.b)Group III after treatment.

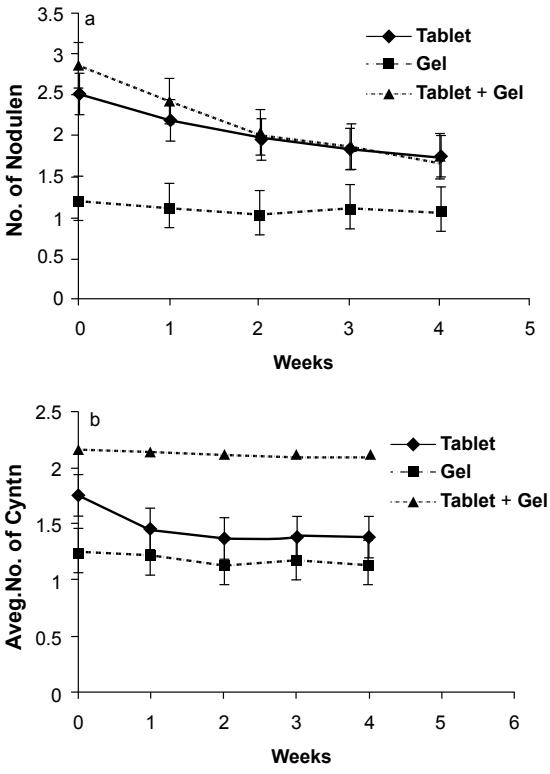


**Figure 7:** Change in no. of deep lesions with time with all treatment groups (a) Cysts (b) Nodules (n=48) *P<0.05 tablet, #P<0.05 gel, @P<0.05 tablet+gel.

Mild acne is characterized by the presence of few to several papules and pustules (without nodules). Patients with moderate acne have too many papules and pustules (along with a few to several nodules) and with severe acne, patients have numerous or extensive papules and pustules (as well as many nodules). Acne is also classified by lesion type as comedonal, papulopustular and nodulocystic [18].Tea tree oil (an essential oil of the native Australian tree *Melaleuca alternifolia*) has been used as a topical antiseptic agent [19]. The studies have shown that tea tree oil can be used in treatment of acne vulgaris [20].

Infact, topical application of 5% tea tree oil has been shown to be equivalent to 5% Benzoyl peroxide in efficacy. Moreover, the use of tea tree oil is associated with much lesser side effects [15].

*Azadirachta indica* contains many essential oils that have antipyretic and antihelmintic properties [21]. It helps in controling the biliary secretion and purifies the blood. It is a good remedy for splenic enlargement [22].Some Indian herbs including *Curcuma longa, Azadirachta indica* have been shown to have anti-inflammatory effect by suppressing the Propionibacterium acnes [23] induced ROS (reactive oxygen species) and pro-inflammatory cytokines [1,23]. Due to this pharmacological activity, these herboformulation are may be used in the treatment of Acne.

This direct anti-inflammatory property is considered to be the basis for the clinical effect of these herbs in treating acne. These herbs act as in the similar manner as the Azelaic acid, which is use in the treatment of Acne as oral antibiotic [4]. Topical and oral preparations of Indian herbs (*Maelaleuca alerternifolia, Curcuma longa, Azadirachta indica and Piper nigrum)* are efficacious in treatment of Acne [24]. The combination of use of internal and external preparation showed better efficacy as compared to the use of oral formulation alone.

All the three treatment arms demonstrated improvement in both

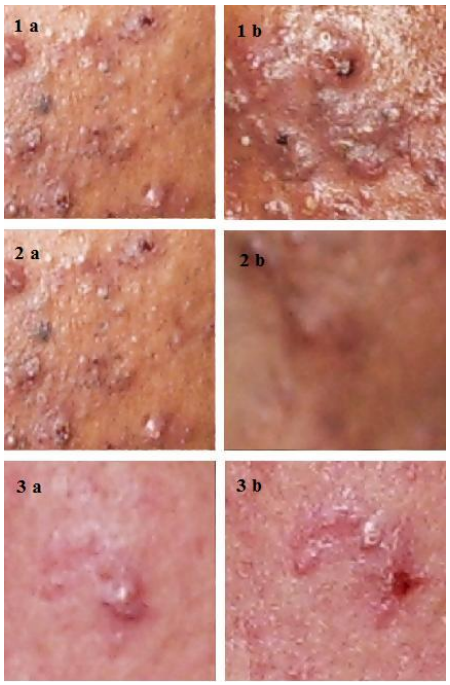


**Figure 8:** Shows the Presence of Nodules before the treatment and after the treatment in all the treatment group (1.a) Group I before treatment (1.b) Group II after treatment, (2.a) Group II before treatment (2.b) Group II after treatment,(3.a)Group III before treatment (3.b)Group III after treatment.

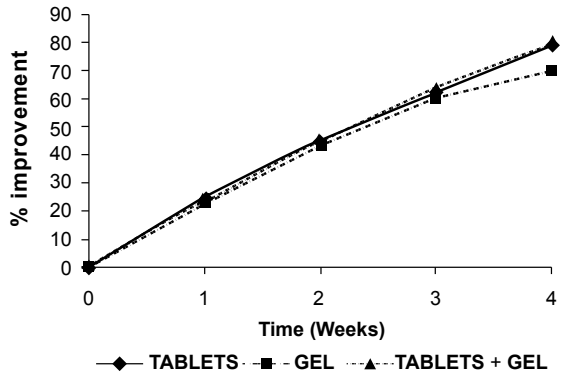


**Figure 9:** Comparative evaluation of non inflamed lesion in all the three treatment group.

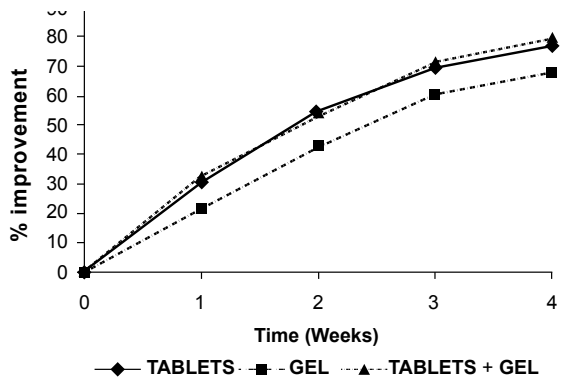


**Figure 10:** Comparative evaluation of inflamed lesion in all the three treatment group.

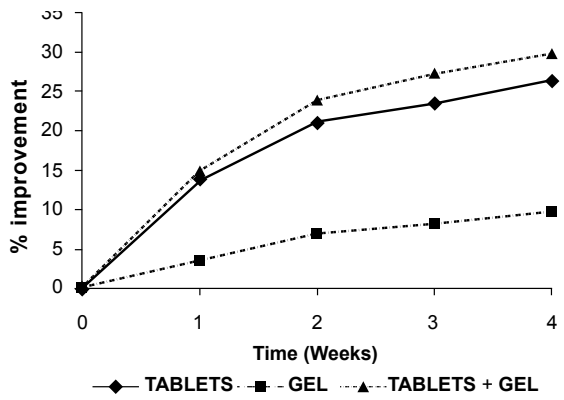


**Figure 11:** Comparative evaluation of deep lesion in all the three treatment group.

non-inflamed and inflamed lesions including superficial and deep ones. For non inflamed lesion (superficial lesions) the improvement with perfact face tablets and perfact face tablets +gel was almost identical. The improved observed with perfact face gel alone was slightly lower at the end of 4 weeks of therapy as compared to other arms (Figure 8).

The difference in the improvement in inflamed lesions (papules and pustules) was slightly more evident between the treatment arms containing tablets (with or without gel) and gel only. There was a difference of about 9.21% in the improvement percentage of treatment arms containing tablet and treatment arm without tablet at end of 4 weeks of therapy. The group I shows the significant Improvement in the inflamed lesions as compared to group II. The group III shows more effect (12%) as compared to group II. It was concluded that group III having more significant effect on the inflamed lesion as compared to group I and II treatment (Figure 9).

The maximum disparity in acne improvement is observed in deep inflammatory lesions. It was observed that the difference in acne improvement in treatment arm with only perfact face gel was 17% as compared to subjects in treatment arm with only perfact face tablet. This difference was further elated to 20% when comparing with subjects in treatment arm containing perfact face tablets and gel. All the three treatments viz. Perfact face acne tablets, Perfact face acne gel and Perfact face acne tablets & gel showed statistically significant reduction in total inflamed lesions i.e. papules and pustules at 2nd and 4th week of therapy as compared to total inflamed lesions on the day of screening of subjects (Figure 10). Cardiff acne disability index was found significantly improved at the end of the therapy with all the three treatments viz. Perfact face acne tablets, Perfact face acne gel and Perfact face acne tablets & gel. No clinically significant change in any of the biochemical parameter is observed in any of the treatment group. There was no difference among the three treatment arms. It was concluded that four weeks of therapy with Perfact face acne tablets and Perfact face acne gel has no effect on hematological profile of the subject including liver and kidney function tests.

## Conclusion

Data reported in this study clearly show that the improvement observed with Perfact face acne gel alone was slightly lower at the end of 4 weeks of therapy as compared to when given along with Perfact oral tablets or when Perfact oral tablets given alone. The efficacy of group III treatment was more as compare to group I and II treatment. The safety parameters remained same before and after the therapy. There were no deaths or serious adverse events. The interim result of the study indicates that perfact face oral tablet and perfact face gel were well tolerated.

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