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A RANDOMIZED SINGLE BLIND PLACEBO CONTROLLED CLINICAL STUDY TO EVALUATE EFFICACY OF AMALAKI (*EMBLICA OFFICINALIS*) EXTRACT CAPSULE ON ACNE VULGARIS ALONG WITH ITS ANTI-OXIDANT PROPERTY

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ABSTRACT: Background and Objectives: *Acne vulgaris* is a chronic skin infection affecting the majority of teenagers and adolescents. It is a disease that affects almost 80% of individuals. Acne, by definition, is multi-factorial chronic inflammatory disease of the Pilosebaceous unit. Nowadays, herbal formulations are gaining popularity in the treatment of various diseases. By considering this fact, the present study was undertaken to prove the potential of Amalaki Capsule in the treatment of Acne. **Methods:** 24 patients were equally divided into two groups. One group (Trial group) was given two Amalaki capsule (each containing 250mg standardized extract) twice daily after meal for 60 days, while the other 12 patients (Control group) received two capsules of maize starch powder twice a day after meal for 60 days. **Results:** All 24 patients completed the treatment undertaken. No drop-out was observed. Highly significant ($P < 0.001$) effect was observed in Skin Hydration, Acne count, and Severity score in comparison to the Control group. The trial drug (Amalaki capsule) also showed good anti-oxidant property through different biochemical parameters. **Conclusion:** In the present placebo-controlled comparative clinical study, the Trial drug (Amalaki capsule) has effectively improved Skin hydration and reduced Acne count and Severity in Acne vulgaris patients. An increase in Total Anti-oxidant Capacity level and a decrease in IgE level shows that the Amalaki capsule has a potent Anti-oxidant effect.

INTRODUCTION: Acne vulgaris is a chronic skin infection affecting the majority of teenagers and adolescents. It is a disease that affects almost 80% of individuals. Acne, by definition, is a multifactorial chronic inflammatory disease of Pilosebaceous unit [1].

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There are multiple causative factors responsible for this infection. Various new therapeutic treatment modalities, including topical applications, systemic oral antibiotics, hormonal therapies, are taken into practice depending upon the need. The response of the patients to these treatments also differs.

All these treatments have their own limitations and drawbacks. In this regard, plant-based products are gaining more popularity due to their advantages like better tolerance, less side effects, and cost-effectiveness. Thus, there is an immense potential for medicinal plants used in various traditional systems.

Among the several herbs, *Phyllanthus emblica* Linn. or *Emblica officinalis* Gaertn., commonly known as Indian gooseberry or Amalaki is one of the most important medicinal herbs possessing multiple therapeutic activities. Amalaki is highly nutritious and is one of the richest sources of vitamin C, amino acids, and minerals [2]. Phyto chemical studies on Amalaki have disclosed major chemical constituents, including tannins, alkaloids, polyphenols, vitamins, and minerals. Pharmaco-logical research reports on Amalaki reveal its analgesic [3], antitussive, immune-modulatory [4,] free radical scavenging [5], anti-oxidant [6,] and anti-inflammatory [7] properties. In addition, it has been shown to reduce cholesterol levels in experimental animals [8] and in clinical studies [9]. In the present study, the efficacy of the Amalaki capsule was evaluated in patients with Acne vulgaris for its anti-oxidant property.

MATERIALS AND METHODS:

Methodology: In the present study, total 24 patients suffering from Acne vulgaris of age between 15-40 years were selected for the study on the basis of inclusion criteria. The patients were divided into two groups *viz.*, the control group and the trial group, with 12 patients each.

Inclusion Criteria:

- Males and Non-pregnant, Non-lactating female of any ethnic group
- 15-40 years of age (both inclusive) at the time of signing the informed consent.
- Patients are having atopic eczema according to Global Acne Grading System.

Exclusion Criteria:

- Patient has clinical dermatitis with infection at the baseline visit.
- Patient with known hypersensitivity to inactive / excipients of the drugs.
- A patient with very severe acne boils requiring systemic therapy/pus drain / surgical dressing.
- Any dermatological condition is other than Acne vulgaris that, in the Investigators opinion, may interfere with the prime evaluation.
- Females who are pregnant, lactating or likely to become pregnant during the study.
- Patients diagnosed with severe systemic disorders.

Trial Drug: Amalaki Capsule (Trade Name: amVigaour Capsule)

Composition: Each hard gelatin capsule contains

S. no.	Ingredients	Part used	Quantity	Reference
1	*Amalaki* (*Emblica offiicinalis*) Extract	Fruit	250 mg	Bhavprakash Pg No. 10
2	Excipients	--	Q.S.	--

Procurement of Trial Drug: Amalaki (*Emblica officinalis*) Capsule registered with the trade name amVigaour Capsule was developed and supplied by K. Patel Phyto extraction Pvt. Ltd.

Study Design: Out of 24 patients, 12 patients (Trial group) were given two Amalaki capsules (250 mg) twice daily after meal for 60 days, while the other 12 patients (Control group) received two capsules of maize starch powder twice in a day after meal for 60 days.

The test was ethically approved by the Institutional Clinical Ethics Committee of Alva's Ayurveda Medical College with letter no. ICEC/AAMC/ 2016/OL/32/33 dated 07.07.2016.

Criteria for the Assessment: The patients were evaluated on the basis of subjective as well as objective parameters.

Subjective Parameters: These are non-laboratory parameters assessed by the investigator. The subjective parameters utilized in this study are:

1. Skin hydration: Measured by skin hydrometer

2. Acne Global Severity Score: This score is a tool used to measure the severity and extent of Acne vulgaris.

3. Dermatology Life Quality Index (DLQI): These subjective parameters were assessed before starting the trial, after 15 days of trial, after 30 days of trial, and after 60 days of trial, respectively. The results obtained were statistically analyzed.

Objective Parameters: These include Laboratory Parameters, which are as followed:

1. IgE levels of the subjects/volunteers

2. TAC levels of the subjects/volunteers

These objective biochemical investigations were performed before starting the treatment as well as after completion of the treatment (*i.e.*, at the end of 60 days).

Adverse Drug Reaction: Adverse drug reactions (if any) were monitored throughout the study.

Statistical Analysis: Statistical Analysis of the results was done under two headings *viz.* Subjective and Objective Parameters. Subjective parameters were assessed four times during the trial, and hence they were tested within the groups using the One-way ANOVA test (F-test). If the statistical significance of any subjective parameter was found in both Control and Trial groups, then paired t-test was applied to compare the results. If any one of the control and trial was not statistically significant, then no further statistical test would be done.

The objective parameters had only two sets of data, *i.e.*, before and after treatment. Hence, they were tested with a 'paired t-test' to check the effect of the treatment within the group, and if the normality test of data is failed, then Wilcoxon Signed Rank Test was used. Unpaired t-test was used to check the difference of effects of both control and trial groups, and if the normality test failed, then the Mann-Whitney U-test was utilized.

Values were expressed in Mean ± SD. P<0.05was considered as statistically significant, P< 0.01 was considered as statistically highly significant, and P< 0.001 was considered as very highly significant.

RESULTS: The study included 24 patients with Acne vulgaris. Out of 24 patients enrolled for the clinical trial, 20 were females, and 4 were males. The patients who were enrolled for the clinical study in the trial group had a history of Acne vulgaris and were between the age group of 20-24 years. No untoward events were observed during the clinical study, and all the participants completed the trial successfully. The data were collected and statistically analyzed.

The Wilcoxon signed-rank method was used to check the significance of the subjective criteria, and the 'paired t-test' was used for objective criteria in a single group. To compare the effect of therapy of two groups, chi-square test carried out for subjective criteria, and 'unpaired t-test' for objective criteria.

Subjective Parameters:

Skin Hydration: Statistical analysis of parameter Skin hydration revealed that the control group is not having any effect on Skin hydration, whereas the trial group has shown statistically highly significant improvement (P<0.01) in Skin hydration. Comparison between Trial and Control group is depicted in **Fig. 1**, **Table 1** and **2**.

The control group showed no significant increase in skin hydration with a *P-value* greater than 0.05, while the trial group showed a significant increase in Skin hydration with P-value less than 0.01. This suggests that the medicine used in the trial group had increased Skin hydration which is statistically significant. Since the only trial group had statistically significant changes, comparison of both the groups together was not undertaken

TABLE 1: EFFECT ON SKIN HYDRATION IN CONTROL GROUP

Group	N	Mean	Std. Dev	P value
Sk.Hyd - BT	12	1.830	0.71	P > 0.05
Sk.Hyd-15 days	12	2.16	0.57	
Sk.Hyd-30 days	12	2.16	0.57	
Sk.Hyd-60 days	12	2.081	0.51	

* One-way ANOVA f-test (comparison within the group)

TABLE 2: EFFECT ON SKIN HYDRATION IN TRIAL GROUP

Group Name	N	Mean	Std. Dev	P Value
Sk.Hyd - BT	12	1.917	0.515	P < 0.01
Sk.Hyd-15 days	12	2.167	0.577	
Sk.Hyd-30 days	12	2.417	0.515	
Sk.Hyd-60 days	12	2.667	0.492	

* One-way ANOVA f-test (comparison within the group)

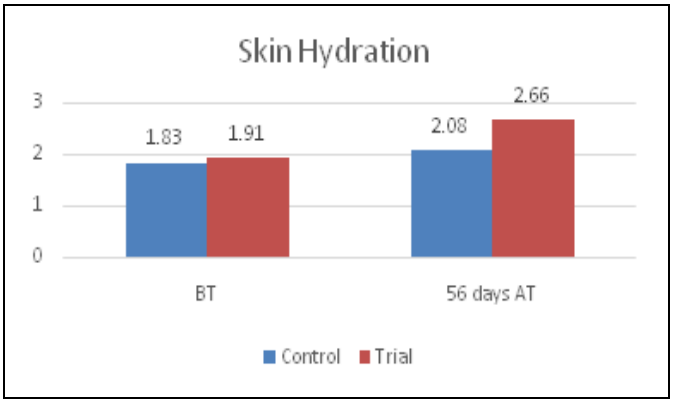

FIG. 1: COMPARISON BETWEEN CONTROL AND TRIAL GROUP ON SKIN HYDRATION

Acne Count and Severity Score: Control group did not show any effect on Acne count and Severity score (P>0.05). In contrast, trial group exhibited a better effect on Acne count and Severity score by reducing the Acne count and severity with high statistical significance (P<0.001).

Data is as shown in **Fig. 2**, **Tables 3** and **4**. This suggests that the medicine used in the trial group had decreased Acne Count and Severity, which is statistically significant. Since the only Trial group had statistically significant changes, a comparison of both the groups together was not undertaken.

TABLE 3: EFFECT ON ACNE COUNT AND SEVERITY SCORE IN CONTROL GROUP

Group	N	Mean	Std. Dev	P value
Acne count - BT	12	3.25	0.75	P > 0.05
Acne count -15 days	12	3.00	0.60	
Acne count -30 days	12	2.83	0.57	
Acne count -60 days	12	2.83	0.57	

* One-way ANOVA f-test (comparison within the group)

TABLE 4: EFFECT ON ACNE COUNT AND SEVERITY SCORE IN TRIAL GROUP

Group	N	Mean	Std. Dev	P value
Acne count - BT	12	2.25	0.45	P < 0.001
Acne count -15 days	12	2.16	0.39	
Acne count -30 days	12	2.16	0.39	
Acne count -60 days	12	1.16	0.57	

* One-way ANOVA f-test (comparison within the group)

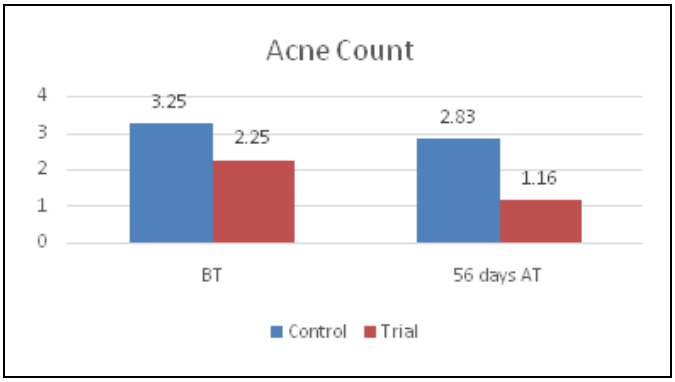

FIG. 2: COMPARISON BETWEEN CONTROL AND TRIAL GROUP ON ACNE COUNT

Dermatology Life Quality Index (DLQI) Levels: A change in DLQI levels was found in both the groups, but the changes in both the groups were statistically not significant. Findings are depicted in **Fig. 3**, **Table** 5 and **6**. Hence, both Control and Trial groups had no statistically significant changes in DLQI, *i.e.*, the Trial drug couldn't show any change in DLQI. Since both the groups had statistically insignificant changes, further comparison of both the groups was not done.

TABLE 5: EFFECT ON DERMATOLOGY LIFE QUALITY INDEX IN CONTROL GROUP

Group	N	Mean	Std. Dev	P value
DLQI - BT	12	2.33	2.99	> 0.05
DLQI -15 days	12	2.25	3.10	
DLQI -30 days	12	2.33	3.33	
DLQI -60 days	12	2.41	3.44	

* One-way ANOVA f-test (comparison within the group)

TABLE 6: EFFECT ON DERMATOLOGY LIFE QUALITY INDEX SCORE IN TRIAL GROUP

Group	N	Mean	Std. Dev	P value
DLQI - BT	12	4.33	3.05	> 0.05
DLQI -15 days	12	4.00	3.13	
DLQI -30 days	12	4.41	2.64	
DLQI -60 days	12	4.16	2.72	

* One-way ANOVA f-test (comparison within the group)

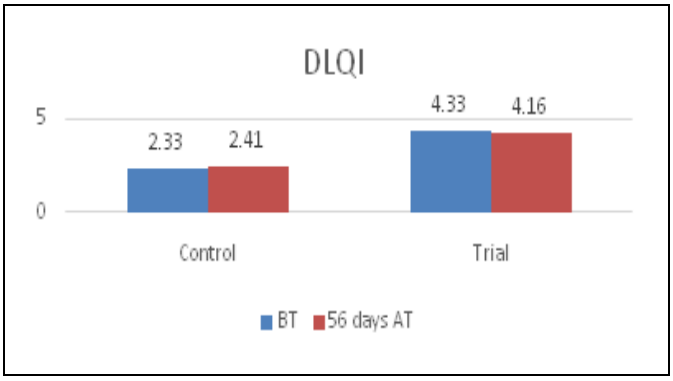

FIG. 3: COMPARISON BETWEEN CONTROL AND TRIAL GROUP ON DLQI

Objective Parameters:

IgE Levels: Slight significant change was observed on the IgE Levels before and after treatment in the control group. The trial drug had significantly decreased the IgE Levels during the treatment.

In comparison with the control group, the trial group showed marked improvement in IgE levels. Findings of both trial and control groups are as depicted in **Fig. 4**, **Table 7** to **9**.

Also, the comparison of both the groups with unpaired t-test **Table 9** shows that there is a significant difference between the effects of both control and trial drugs. The trial drug had better performed in reducing the IgE levels.

TABLE 7: EFFECT ON Ig E IN CONTROL GROUP

Group	N	Mean	Std. Dev	P value
C - IGE - BT	12	403.003	359.928	
C - IGE - AT	12	402.702	360.210	P<0.05
Difference	12	0.301	0.429	

* Paired t-tests (comparison within the group)

TABLE 8: EFFECT ON Ig E IN TRIAL GROUP

Group	N	Mean	Std. Dev	P value
T - IGE - BT	12	500	430.04	
T - IGE - AT	12	401	394.62	<0.001
Difference	12	99	243.22	

* Paired t-tests (comparison within the group)

TABLE 9: EFFECT COMPARISON OF BOTH GROUPS ON IG E

Group	N	Mean	Std. Dev	P value
C- IGE- BT-AT	12	0.301	0.429	<0.001
T- IGE - BT-AT	12	99.000	243.2	

* Un-paired t-tests (comparison between the groups)

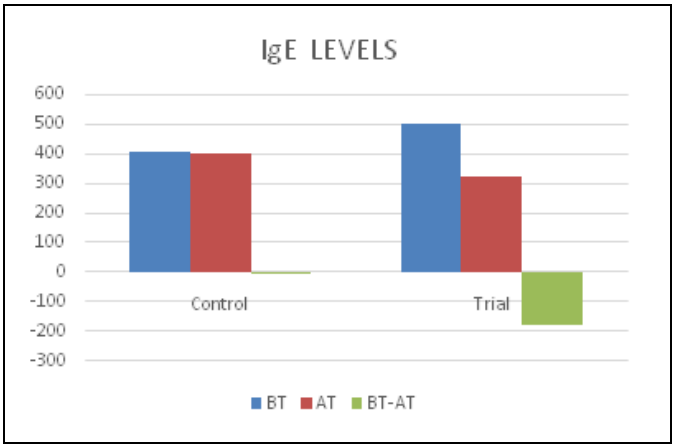

FIG. 4: COMPARISON BETWEEN CONTROL AND TRIAL GROUP ON IGE LEVELS

Total Antioxidant Capacity (TAC) Levels: No change was observed on the TAC Levels before and after treatment in the control group.

Statistical analysis revealed insignificant improvement with P>0.05. The trial drug had increased the TAC Levels to a markable range with very highly significant improvement with P<0.001.

In comparison with the control group, the trial group had shown marked improvement in TAC Level. Findings of both trial and control groups are as depicted in **Fig. 5**, **Table 10** to **12**.

Also, the comparison of both the groups with 'unpaired t-test' **Table 12** showed a significant difference between the effects observed in both control and trial groups. The trial drug has performed better in increasing the TAC levels.

TABLE 10: EFFECT ON TAC LEVEL IN CONTROL GROUP

Group	N	Mean	Std. Dev	P value
C - TAC - BT	12	824.083	199.127	
C - TAC - AT	12	823.833	200.248	P>0.05
Difference	12	0.250	4.288	

* Paired t-tests (comparison within the group)

TABLE 11: EFFECT ON TAC LEVEL IN TRIAL GROUP

Group	N	Mean	Std. Dev	P value
T - TAC - BT	12	876.583	193.762	
T - TAC - AT	12	1098.667	210.384	<0.001
Difference	12	-222.083	86.706	

* Paired t-tests (comparison within the group)

TABLE 12: EFFECT COMPARISON OF BOTH GROUPS ON TAC LEVEL

Group	N	Mean	Std. Dev	P value
C- TAC- BT-AT	12	0.25	4.288	<0.001
T- TAC - BT-AT	12	222.08	86.706	

* Un-paired t-tests (comparison between the groups)

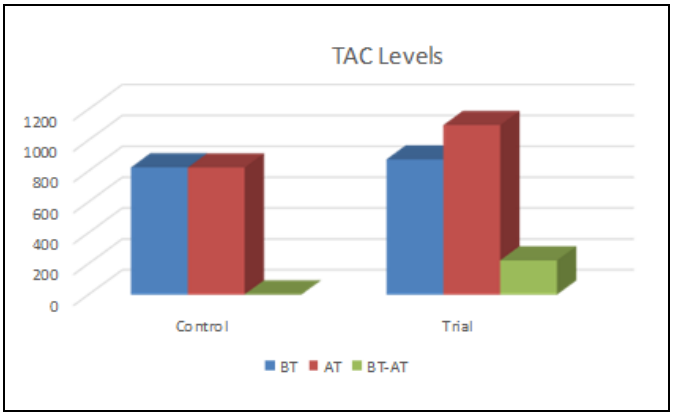

FIG. 5: COMPARISON BETWEEN CONTROL AND TRIAL GROUP ON TAC LEVELS

Adverse Drug Reaction Due to Treatments: None of the patients receiving either Amalaki capsule or Placebo therapy reported any adverse drug reaction during the treatment or two weeks later.

DISCUSSION: Acne is one of the prevalent dermatologic diseases affecting mainly teenagers and adolescents. Various new therapeutic modalities are in practice having certain drawbacks and side effects. The present study was an attempt to evaluate the efficacy of Amalaki capsule in Acne vulgaris with its Anti-oxidant property.

In Ayurveda, Amalaki is reported to be beneficial in various ailments. Various experimental studies also have suggested the antioxidant [10] effect of Amalaki.

In this clinical study, Anti-oxidant property of Amalaki has been reported in patients aged 35-55 years. In the present study, the trial drug Amalaki capsule was administered as 250 mg – 2 capsules per day for 60 days. The starch capsule was used as placebo in the control group for 60 days.

Among the subjective parameters, the trial drug Amalaki capsule had shown statistically highly significant improvement in skin hydration level ($P<0.01$) and very highly significant improvement ($P<0.001$) in Acne count and severity in comparison with the Control group.

The inflammation and Acne count was reduced after the treatment. No significant improvement was observed with DLQI level. The control drug has not shown any effect after the treatment statistically. Among the objective parameters, the Trial drug had reduced the IgE level after the treatment to a moderate range which statistically has a very highly significant level ($P<0.001$). The total Anti-oxidant capacity (TAC) level was increased to a remarkable range ($P<0.001$).

Amalaki contains high amounts of vitamin C in the natural form as well as cytokine-like substances identified as zeatin, Z-riboside, Z-nucleotide, flavonoids pectin, and 30% tannins. Tannins present in Amalaki retard the oxidation of vitamin C, while pectin has been reported to decrease serum cholesterol levels in human beings [11.]

The flavonoid content of Amalaki was analyzed for its biological activity and found to possess a potent hypolipidemic effect though the exact mechanism of hypolipidemic action of Amalaki is not known, it is likely that the Amalaki induced favorable changes in the lipid profile may be due to several mechanisms such as an interference with cholesterol absorption [8] inhibition of HMG Co-A reductase activity and increase in Lecithin-Cholesterol Acyltransferase (LCAT) activity [12].

In the present study Amalaki capsule reduced the Acne count and severity; even though no remarkable findings were noticed with DLQI parameters. These findings may be due to the small number of patients included under this study, which might have influenced the statistical analysis outcome. An increase in TAC level and reduction in IgE level proved anti-oxidant effect of Amalaki capsule.

CONCLUSION: In the present placebo-controlled comparative clinical study, the trial drug Amalaki capsule has effectively improved skin hydration and reduced Acne count and severity in Acne vulgaris patients. An increase in TAC level and decrease in IgE level shows that the Amalaki capsule has a potent Anti-oxidant effect.

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CONFLICTS OF INTEREST: Nil (No conflict between two organizations)

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