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Research paper

Evaluation of the effectiveness of Eladi Keram for the treatment of Acne vulgaris: a randomised controlled pilot study

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ABSTRACT

Introduction: Acne is a multifactorial and common skin disease which can significantly affect the quality of life of sufferers. In this study, a topical herbal preparation traditionally used in Ayurvedic medicine was evaluated as a treatment for individuals with acne on their shoulders and backs.

Methods: Study participants were randomly assigned either to treatment (Eladi Keram) or vehicle control (coconut oil) groups under double blind conditions and instructed on its daily home application. Standardised lesion counting and acne grading were conducted in accordance with US Food and Drug Administration guidelines and with reference to the Leeds Acne Grading Technique. Participants were assessed for severity of the condition at commencement and on day 28 of treatment.

Results: The treatment group showed improvements of 42% ($p < 0.005$) on the Investigators Global Assessment scale, a 60% ($p < 0.05$) reduction in inflammatory lesions, a 59% ($p < 0.05$) reduction in non-inflammatory lesions, and a 59% ($p < 0.005$) reduction in combined lesion count. The control group showed no statistically significant changes for these criteria.

Conclusion: This study is the first reported clinical evaluation of Eladi Keram as a treatment for acne and findings suggest that it could be effective in reducing inflammatory and non-inflammatory lesions, warranting further investigation by means of a larger scale clinical trial.

1. Introduction

Acne vulgaris is a common chronic skin disease, predominant in adolescence but also affecting a large number of adults [1–3]. Although acne is not associated directly with mortality or conventionally defined morbidity, the discomfort, risk of scarring and often strong emotional distress associated with the condition means it is increasingly considered a valid target for treatment rather than a condition to be endured [4,5]. Acne is defined by the presence of inflamed red papules, pustules, comedones (black or whiteheads) and the pathogenesis of the condition involves a complex sequence of events, including sebum production, hyperkeratinisation, poral occlusion, colonisation by *Propionibacterium acnes* (*P. acnes*) bacteria and a persistent inflammatory immune response [6]. Microcomedones are often the initial subclinical acne lesions which further mature into non-inflammatory comedones and/or inflammatory lesions [7,8]. The development of microcomedones occurs via hyperkeratinisation (keratin/infundibular plug) in the follicular infundibulum and sebaceous ducts [8]. Follicular epithelial hyperproliferation leads to hyperkeratosis and eventually to the formation of microcomedones and this may be promoted by increased sebum production. Hyperkeratosis is characterised by increased number and size of keratohyaline granules, lipid droplet accumulation, and epidermal scale/keratin flakes [9]. Consequent alteration in lipid composition of sebum, bacterial overgrowth, and hormonal factors elicit stimulation of the immune and inflammatory responses via the action of $CD3^+$, $CD4^+$ (lymphocytes) and macrophages [6,8,9]. The local overproduction of androgen hormones including testosterone, dehydroepiandrosterone sulfate, and dihydrotestosterone can regulate sebaceous gland growth and sebum production and consequently the formation of acne lesions [7,9–11]. Furthermore, androgen is involved in comedogenesis and hyperkeratinisation via regulating growth factors and IL-1α [8]. Insulin-like growth factor-1 production, stimulated by growth hormone, acts on sebaceous glands by causing their growth and stimulating lipogenesis [7–9]. Under certain circumstances, *P. acnes*, a common commensal Gram-positive anaerobic bacterium (usually a benign inhabitant of sebaceous follicles) may act directly or indirectly on pilosebaceous ducts and activate certain inflammatory proteins (including the pro-inflammatory cytokines) [12] causing inflammation and hyperkeratinisation [8]. However, it has also been reported that comedones can develop in the absence of *P. acnes* [13].

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Table 1
Herbs used in the formulation of Eladi Keram and their reported actions.

Scientific name	Sanskrit name	Anti-bacterial	Anti-inflammatory
Actiniopteris dichotoma Kuhn (Actiniopteridaceae)	Dhyamakam		
Amomum subulatum Roxb. (Zingiberaceae)	Brihadela	[24]	[24]
Aquilaria agallocha Roxb. (Thymelaeaceae)	Agaru	[25]	
Banksea speciosa J.Koenig (Costaceae)	Pushkarmula		
Boswellia glabra Roxb. (Burseraceae)	Saamprani		
Boswellia serrata Roxb. (Burseraceae)	Thurushkam	[26]	[27,28]
Callicarpa macrophylla Vahl (Lamiaceae)	Priyangu		[29]
Calophyllum inophyllum L. (Clusiaceae)	Thejovathy/Punnag		[30–32]
Cedrus deodara Roxb. (Pinaceae)	Devadaru	[33]	[34]
Cinnamomum tamala T.Nees & Eberm. (Lauraceae)	Pathram		[35]
Cinnamomum zeylanicum Blume (Lauraceae)	Twak	[36*,37]	[38]
Coleus vettiveroides K.C.Jacob (Lamiaceae)	Hreeberam		[39]
Commiphora mukul Engl. (Burseraceae)	Gulgulu		[40]
Commiphora myrrha Engl. (Burseraceae)	Rasam (Narum pasha)	[41]	[42]
Crocus sativus Ten. (Iridaceae)	Kumkumam[a]		[43,44]
Elletaria cardamomum Maton (Zingiberaceae)	Elavakulam	[45–47]	[48]
Ipomoea pes-tigridis L. (Convolvulaceae)	Vyagranakhi	[49] *	[50]
Kaempferia galanga L. (Zingiberaceae)	Sati		[51,52]
Mesua ferrea L. (Clusiaceae)	Nagakesaram	[53]	[54]
Myristica fragrans Houtt. (Myristicaceae)	Jaathiphalam	[55]	
Nardostachys jatamansi C.B.Clarke (Valerianaceae)	Maanchi	[56]	[57]
Pinus roxburghii Sarg. (Pinaceae)	Sreevasakam	[58]	[59]
Polygonum alatum Buch. (Polygonaceae)	Sprukka	[60]	
Saussurea lappa (Decne.) C.B.Clarke (Asteraceae)	Kushtam	[61]	[62]
Shorea robusta C.F.Gaertn. (Dipterocarpaceae)	Sarjarasam		[63,64]
Taxus baccata Thunb. (Taxaceae)	Thaleesa pathram		[65]
Valeriana wallichii DC. (Valerianaceae)	Thagaram	[66]	[66]
Oyster shell (Ostreidae)	Sukthi[b]		[67]

The ingredients list was supplied by Nagarjuna Ayurvedic Group, Kalayanthani P.O., Thodupuzha, Kerala, India.
All components of Eladi Keram were present at % concentrations of 0.44% (w/v) with the exception of Kumkumam[a] at 0.17% (w/v) and Sukthi[b] at trace levels.
* Anti-bacterial effect against *Propionibacterium acnes* [exhibited by two of the constituents; Twak and Vyagranakhi].

A range of conventional treatments for acne exist including oral and topical retinoids, antibiotics, benzoyl peroxide and hormonal treatments [14], but concerns over side effects of retinoids including severe depression [15] and the development of antibiotic resistance to *P. acnes* [16] have created an appetite for novel treatments, including the use of herbal preparations [17,18].

Eladi Keram is a commercially available Ayurvedic herbal formulation with a long standing anecdotal evidence base as an effective treatment for various skin conditions including acne (referred in classical Ayurvedic text as “pidaka” a form of Kushta (skin disease)) [19,20]. The fact that this ancient formula (Eladi Keram) is still widely manufactured and prescribed by Ayurvedic practitioners, highlights the cultural importance of these formulations to the rich ethnopharmacological tradition of Indian medicine. Although Eladi Keram has a long standing anecdotal evidence base as an effective treatment for various skin conditions, prior to this study, there has been no reported clinical evaluation using a biomedical model of research. It is on this basis together with interest in novel treatments and potential reduced side effects of herbal remedies that Eladi Keram was deemed worthy of investigation

2. Materials and methods

2.1. Study design and study groups

A randomised controlled pilot study was conducted to evaluate the effectiveness of Eladi Keram for participants with acne on their shoulders and backs in a double-blinded clinical observation. Eladi Keram was selected for the study because it met our selection criteria of being a commercially available traditional medicine with long-standing use, and with claims of efficacy by traditional medicine practitioners and users. The study deliberately focused on subjects with acne on the shoulders and backs rather than on the face. Although greater emotional distress is associated with facial acne [3] and therefore its targeting may be more beneficial, this is countered by the greater likelihood of participants self-treating and/or masking facial acne during the trial. This would lead to the increased possibility of introducing confounding variables in such subjects suggesting that a study on back and shoulder acne would in practice be more scientifically robust. Moreover, any potential benefits noted in the treatment of back and shoulder acne are also likely to be relevant to subjects with facial acne.

There is a higher prevalence of acne in 15–24 year olds but some older people have been confirmed as sufferers as evidenced by UK GP returns analysis [21]. In this study, under 18 year olds were excluded from the study due to ethical and recruitment issues. The present clinical observation study was conducted on participants, aged 19 − 50 (mean = 30.05 and median = 30), reporting acne on shoulders or chest unless they reported the following exclusion criteria: being pregnant, breast feeding, taking other medication for acne, using sun tanning lamps/planning travel to sunny climates, or reporting shellfish allergy. A power calculation (see Statistical analysis) indicated that approximately 20 participants were required to demonstrate a statistically significant and clinically meaningful reduction in acne. From 24 enquiries, three recruits did not fulfil the inclusion criteria. A total of 21 participants (6 male and 15 female) therefore were enrolled. Ten were randomly (using Minitab ® statistical software random data sampling function (Minitab Ltd. Coventry, U.K.)) assigned to the treatment group and eleven to the control group.

Ethical approval was granted by Middlesex University Ethics Natural Sciences Sub-Committee and written informed consent was obtained from each participant prior to study commencement.

2.2. Test samples

Eladi Keram was purchased from Nagarjuna Ayurvedic Group (http://www.nagarjunaayurveda.com/) and the constituent herbs were authenticated by the manufacturers using thin layer chromatography