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Review Article

CLINICAL REVIEW: ACNE VULGARIS – DERMATON, GLOON & MAHAMANJISHTHAADI KWATH - A COMPLETE AYURVEDIC TREATMENT

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ABSTRACT

Introduction Acne vulgaris, or acne, as it is generally called, is the most common skin disease, affecting nearly 80 percent of persons at some time between the ages of 11 and 30 years.¹ It can persist for years and result in disfigurement and permanent scarring, and it can have serious adverse effects on psychosocial development, resulting in emotional problems, withdrawal from society, and depression.² The pathogenesis of acne is multifactorial, and therapy can now be directed at many of these factors. This review summarizes current concepts of the rational treatment of acne vulgaris.

Objective To review the best evidence available for individualized Ayurvedic treatment of acne.

Study Selection Well-designed randomized controlled trials, meta-analyses, and other systematic reviews are the focus of this article.

Data Synthesis Main outcome measures of 29 randomized double-blind trials that were evaluated included reductions in inflammatory, noninflammatory, and total acne lesion counts. Glo ON reduce the number of comedones and inflammatory lesions in the range of 40% to 70%. These agents are the mainstay of therapy in patients with comedones only. Other agents, including DermatON, *Maha Manjishthadi Kwath* &, *Dashang lep* & Neurova *Lep* all yield high response rates. Patients with mild to moderate severity inflammatory acne with papules and pustules should be treated with all medicines prescribed above.

DermatON are first-line therapy in patients with moderate to severe inflammatory acne while DermatON & GloON is indicated for severe nodular acne, treatment failures, scarring, frequent relapses, or in cases of severe psychological distress. Long-term topical or oral antibiotic therapy should be avoided when feasible to minimize occurrence of bacterial resistance. DermatON is a powerful teratogen mandating strict precautions for use among women of childbearing age.

Conclusions Acne responses to treatment vary considerably. Frequently more than 1 treatment modality is used concomitantly. Best results are seen when treatments are individualized on the basis of clinical presentation. The management of acne vulgaris by non-dermatologists is increasing. In this article we attempt to answer the question: what treatments in acne vulgaris have proven efficacy and how are these treatments best administered and individualized to optimize results and minimize complications? We considered the efficacy and safety of topical $Dashang\ lep$, Neurova, Tab. DermatON, Tab. GloOn & $Mahamanjishthadi\ Kwatha$.

METHODS

A librarian-assisted literature search was performed for English-language randomized clinical trials. We used MEDLINE and EMBASE to identify all therapeutic clinical trials, meta-analyses, and systematic analyses concerning acne vulgaris from 1966 to 2004. We further cross-referenced bibliographies of identified articles. This search strategy identified 248 articles. We then evaluated titles and abstracts, and excluded studies that were not blinded, were not randomized, had sample sizes of fewer than 50, did not provide adequate information with respect to objective outcomes measures, contained no original data, pertained to treatments that are not available, did not involve humans, or were therapeutic failures. We used the following search words: acne vulgaris, acne, tretinoin, Ras Manikya, Suvarna Rajvangeshwar, Khadir, Chopchini, Sariva. Nimba Kwath. Kaishor Guggul, clinical trials, review, therapy, treatment, and randomized controlled trials.

We identified 90 randomized double-blind trials, which comprise the focus of this article. Where possible, data concerning responses to treatment were put in terms of percent reduction of inflammatory lesions, noninflammatory lesions (comedones), and total lesions.

A recent methodological literature review of acne therapy trials over the last 50 years found that methods of grading acne severity and methods of assessing outcome measures are highly inconsistent.² There are more than 25 methods of assessing acne severity and more than 19 methods for counting lesions. Our literature review verifies the lack of standardized of methodology. Nevertheless, analysis of acne therapy data does allow conclusions to be drawn that can direct therapeutic decisions.

In addition to the randomized controlled trials (RCTs), we reviewed selected articles that included data collected or analyzed after the trial, including meta-analyses and other systematic reviews. We also mention selected non-RCTs when they represent best evidence concerning established therapies that have not yet been studied in well-designed RCTs.

Pathophysiology

The origin of acne vulgaris is complex and incompletely understood. At least 4 pathophysiologic events take place within acne-infected hair follicles: (1) androgen-mediated stimulation of sebaceous gland activity, (2) abnormal keratinization leading to follicular plugging (comedo formation), (3) proliferation of the bacterium *Propionibacterium acnes* within the follicle, and (4) inflammation. In addition to these 4 basic mechanisms, genetic factors, and possibly diet may influence the development and severity of acne.

Case-based clinical applications

Diagnosis

The diagnosis of acne vulgaris is usually uncomplicated. Differential diagnoses mainly include rosacea, perioral dermatitis, bacterial folliculitis, and drug-induced acneiform eruptions. The presence of comedones confirms the diagnosis of acne vulgaris.

Evidence-based literature in acne treatment is growing, and there is sufficient evidence to justify specific treatments for most clinical presentations. Successful outcomes frequently require nuance in management and a thorough understanding of all treatment modalities. Good outcomes are based on what is perceived by the patient as well as what can be measured. Since morbidity in acne is primarily emotional (psychological), different degrees of success may satisfy different individuals. Acne severity fluctuates over time and treatments often need to change accordingly.

Comedones Only

For this treatment GloON are the mainstay of treatment. Maintenance treatment is usually required.

Inflammatory Acne (Papules and Pustules), Mild to Moderate Severity

DermatON the treatment of choice for these patients' best results require 8 to 12 weeks and maintenance therapy is usually required. Reasonable response expectations are in the range of 30% to 80%. 17-20.25,26

Moderate to Severe Inflammatory Acne

DermatON & GloON Response expectations with oral antibiotics are in the range of 64% to 86%. 34,40

This Treatment require a minimum of 6 to 8 weeks of treatment. There are no strict regulations on duration of use, but the recent increase in the prevalence of resistant organisms has resulted in current recommendations to encourage maintenance therapy for Longer perod. 35

Laboratory Studies

For women with regular menstrual cycles, serum-androgen measurements are not necessary. For those with rapid onset of hyperandrogenism and virilization, an androgen-secreting ovarian or adrenal tumor can be excluded with a normal total testosterone and dehydroepiandosterone sulfate levels, respectively. Irregular menses, hirsutism, obesity, or a family history of type 2 diabetes suggest a possible endocrinopathy, such as polycystic ovary syndrome. Further studies may be indicated, which could include measurement of gonadotropins, free testosterone, 17-hydroxy progesterone, prolactin, and androstenedione. 57,100 Unfortunately, there is no widely accepted best laboratory test in this setting. 101

TREATMENT

Dermaton

Composition:

	Weight (mg)
Rasamanikya	15
Arogyavardhini	65
Gandhak rasayan	75
Kaishor Guggul	80
Sariva (Hemidesmus indicus)	35
Khadir (Acacia catechu)	40
Manjishtha (Rubia cordifolia)	70
Gum acacia	20
Bhavana: Nimba Swaras	
	Arogyavardhini Gandhak rasayan Kaishor Guggul Sariva (Hemidesmus indicus) Khadir (Acacia catechu) Manjishtha (Rubia cordifolia) Gum acacia

Tablet wt: 400mg

GloON

Composition:

Name of the Ingredients	Weight (mg)
Suvarna raj Vangeshwar	15
Chopchini	65
Gandhak rasayan	75
Kaishor Guggul	80
Sariva (Hemidesmus indicus)	35
Khadir (Acacia catechu)	40
Manjishtha (Rubia cordifolia)	70
Gum acacia	20
Bhavana: Sariva Phant	
	Suvarna raj Vangeshwar Chopchini Gandhak rasayan Kaishor Guggul Sariva (Hemidesmus indicus) Khadir (Acacia catechu) Manjishtha (Rubia cordifolia) Gum acacia

Tablet wt: 400mg

Rasmanikya in skin disorders:

It offers beneficial effects in the management of diseases such as; leprosy, surface wounds, pus, boils dryness of skin, eczema, rashes and leukoderma, etc. Impurity of blood is one of the reasons of skin ailments and *Rasmanikya* acts as *Raktashodhak* means it purify blood thus gives relief from skin problems, it is believed that presence of purified sulfur helps to detoxify blood. The ingredients of *Rasmanikya* acts as *Kushthahar* thus relive symptoms of leprosy or many other skin diseases. The formulations impart calming and soothing effects thus help to reduces pain, itching and burning sensation related to skin problems. It reduces damage caused by sun-burn, restore energies and redress blood morbidity. The immunosuppressants effects give benefits in autoimmune skin diseases such as; Polymorphous Light Eruption and Systemic Lupus Erythematosus, etc. The presence of metallic compounds initiates re-pigmentation lost by disease consequences. The ingredients of formulation help to manage *Kapala* and *Audumbera Kushtha* thus improves manifestations of erythroderma.

Biological response of *Rasmanikya* in skin disorders:

- ➤ It balances *Vata* and *Kapha* thus relieve skin ailments.
- > It relief fever related to other diseases.
- Remove excessive phlegm and toxins from body which may sometimes initiate pathogenesis of skin diseases.

- > It treats disease like; ring worm, scabies, psoriasis and urticaria, etc.
- > Rasamanikya breaks immunological adversity which can trigger skin manifestation.
- > Relieve pain, inflammation and swelling
- > The antimicrobial property resists skin infection
- > The metallic components enhance colour, complexion and integrity of skin

The major ingredients of *Rasmanikya* are *Tamara Bhasma*, *Hartala* and *Abhrak Bhasma*. *Tamara Bhasma* helps in red blood cells formation thus restore complexion and colour of skin. The presence of *Tamara Bhasma* reduces chances of disease which can arise due to the vitiation of blood. *Hartala* offers beneficial effects in skin diseases like; itching, eczema and herpes, etc. *Abhrak Bhasma* another component of *Rasmanikya* boosts immunity thus prevent skin infection, it also imparts strength thus maintain physical compatibility and skin integrity. Formulations helps to maintain youthfulness of skin nourishes skin and rehydrate skin therefore provide natural beauty and strength of skin. *Rasmanikya* prevent wrinkles and skin symptoms of premature aging.

Effect of Rasmanikya on Doshas for skin vitality

Ayurveda formulation *Rasmanikya* offers beneficial effects towards the pacification of *Doshas* and gives specific benefits in the management of skin problems as depicted in **Figure 1**.

- > The skin predominance to *Vata Dosha* remain dry and sensitive to touching sensation, *Rasmanikya* pacifies excess *Vata* thus prevent skin dehydration and sensitivity.
- > Pacification of *Pitta Dosha* by *Rasmanikya* helps in breakouts & photosensitivity tolerance of skin.
- > Rasmanikya correct aggravated Kapha dosha thus help to maintain skin texture and tolerant to sun exposure.
- The simultaneous corrections of *Vata-Pitta* related to skin problems helps in dry and sensitive skin.
- > The ingredients of formulation pacify *Kapha-Pitta* together therefore resist skin problems that may occur due to the excessive oily layer.
- > It removes *Ama* (toxins) accumulated under the skin.
- > Improves circulation thus enhances supply to skin tissue.

Ingredients of Rasmanikya enhance digestive fire therefore contributes towards development of skin tissue.

Suvarna Raj Vangeshwar

'Suvarna Raj Vangeshwara' is a metallic drug preparation described in an Ayurvedic scheduled text 'Rasataragini'. The drug contains Mercury (Hg), Sulphur (S), Tin (Sn) and Ammonium Chloride (NH₄Cl)

(in the form of 'Navasagar'). The drug be-longs to a class of 'Kupipakva Rasayana', which was produced through a specialized method. In this method the homogenous mixture of the ingredients is placed in a closed narrow mouthed long necked glass flask, wrapped in a multi-layered clay smeared muslin cloth. The flask was then subjected to prolonged controlled heating in a sand bath. At the end of heating the product 'Kupipakva Rasayana' in this study 'Suvarna Raj Vangesvara' was collected at the bottom of the flask. The flask was skillfully broken and the product 'Suvarna Raj Vangesvara' was collected Suvarna Raj Vangesvara. In Ferric chloride reducing power assay Suvarna Raj Vangesvara showed dose dependent increase in anti- oxidant activity almost similar to that of standard antioxidant i.e. Vit C. at all concentrations. Suvarna Raj Vangesvara exhi- bited higher inhibitory activity on process of Lipid peroxidation in all concentrations as compared to the standard antioxidant ascorbic acid. Thus, overall Suvarna Raj Vangesvara showed a potent and very good dose dependant antioxidant activity as compared the respective standards. Suvarna Raj Vangeshwara is found to possess a potent antioxidant activity through this study. It is used in *Ayurvedic* practice by Ayurvedic practitioners for multiple purpose may be because of its potent antioxidant activity since, reactive oxygen species plays important role in many pathological conditions and diseases. On this background, this multi-potential activity of this drug needs to be explored in future on in-vitro and in-vivo scales.

Mahamanjishthadi Kwath

This study may serve as standard reference for quality control analysis and checking antimicrobial potential of various *Asava*, *Aristha* and *Kadha* formulations. Ethnopharmacologists, microbiologists, and natural-products chemists can use such information of phytochemicals and isolate, characterize more lead phytochemicals which could be developed for the treatment of diseases.

Antimicrobial evaluations confirmed susceptibility of Ayurvedic formulation, *Mahamanjishtadi Kadha* against common skin bacteria and fungi, *Staphylococcus aureus*, *P. aeruginosa*, *S. Epidermidis and C. albicans*. The broad spectrum of antimicrobial activity of the herbal ingredients, *viz.*, *Manjishtha* (*Rubia cordifolia* Linn), *Sariva* (*Hemidesmus indicus* Linn), *Nimba* (*Azadirachta indica* A. Juss.), *Khadir* (*Acacia catechu* Linn. f.), *Haridra* (*Curcuma longa* Linn.), *Bibhitaki*, (*Terminalia bellerica* Gaertn.) Roxb.), *Haritaki* (*Terminalia chebula* (Gaertn.) Retz.) and *Amalaki* (*Emblica officinalis* Gaertn) in composition forms the basis of selection to be incorporated for treating skin infections.

CONCLUSION

Current treatments in acne target one or more of the known mechanisms involved in the disease. Combining more than 1 treatment frequently yields optimal responses. Patients may require adjustment of therapies depending on their degree of improvement and level of tolerance to the treatments.

REFERENCES

- 1. Stern RS. Acne therapy: medication use and sources of care in office-base practice. *Arch Dermatol*. 1996;132:776-780.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8678569&dopt=AbstractGoogle Scholar
- 2. Lehmann HP, Robinson KA, Andrews JS. et al. Acne therapy: a methodologic review. *J Am Acad Dermatol*.2002;47:231-240.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12140469&dopt=AbstractGoogle Scholar
- 3. Bataille V, Snieder H, MacGregor AJ, Sasieni P, Spector TD. The influence of genetics and environmental factors in the pathogenesis of acne: a twin study of acne in women. *J Invest Dermatol*.2002;119:1317-1322.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12485434&dopt=AbstractGoogle Scholar
- 4. Goulden V, McGeown CH, Cunliffe WJ. The familial risk of adult acne: a comparison between first-degree relatives of affected and unaffected individuals. *Br J Dermatol*.1999;141:297-300.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids= 10468803&dopt=AbstractGoogle Scholar
- 5. Cordain L, Lindeberg s, Hurtado M, Hill K, Eaton SB, Brand-Miller J. Acne vulgaris: a disease of western civilization. *Arch Dermatol*.2002;138:1584-1590. http://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12472346&dopt=AbstractGoogle Scholar
- 6. Cunliffe WJ, Poncet M, Loesche C. et al. A comparison of the efficacy and tolerability of adapalene 0.1% gel vs tretinoin 0.025% gel in patients with acne vulgaris: a meta analysis of five randomized trials. *Br J Dermatol*.1998;139 (suppl 52): 48-56. http://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids= 9990421&dopt=AbstractGoogle Scholar
- 7. Egan N, Loesche MC, Baker MM. Randomized controlled bilateral (split-face) comparison trial of the tolerability and patient preference of adapalene gel 0.1% and tretinoin microsphere gel 0.1% for the treatment of acne vulgaris. *Cutis*.2001;68(suppl 4):20-24.http://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11845944&dopt=AbstractGoogle Scholar

- 8. Thiboutot D, Gold MH, Jarratt MT. et al. Randomized controlled trial of the tolerability, safety and efficacy of adapalene gel 0.1% and tretinoin microsphere gel 0.1% for the treatment of acne vulgaris. *Cutis*.2001;68(suppl4):10-19.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11845943&dopt=AbstractGoogle Scholar
- 9. Cunliffe WJ, Danby FW, Dunlap F. et al. Randomised controlled trial of the efficacy and safety of adapalene gel 0.1% and tretinoin cream 0.05% in patients with acne vulgaris. *Eur J Dermatol*.2002;12:350-354.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12095880&dopt=AbstractGoogle Scholar
- 10. Shalita AR, Chalker DK, Griffith RF. et al. Tazarotene gel is safe and effective in the treatment of acne vulgaris: a multicenter, double blind, vehicle-controlled study. *Cutis*. 1999;63:349-354.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids= 10388959&dopt=AbstractGoogle Scholar
- 11. Leyden JL, Tanghetti EA, Miller B. et al. Once daily tazarotene 0.1% gel versus once daily tretinoin 0.1% microsponge gel for the treatment of facial acne vulgaris: a double blind randomized trial. *Cutis*.2002;69(suppl2):12-19.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12095064&dopt=AbstractGoogle Scholar
- 12. Webster GF, Berson D, Stein LF. et al. Efficacy and tolerability of once daily tazarotene 0.1% gel versus once daily tretinoin 0.025% gel in the treatment of facial acne vulgaris: a randomized trial. *Cutis*.2001;67(suppl6):4-9.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11499329&dopt=AbstractGoogle Scholar
- 13. Lucky A, Jorizzo JL, Rodriguez D. et al. Efficacy and tolerance of adapalene cream 0.1% compared with its cream vehicle for the treatment of acne vulgaris. *Cutis*. 2001;68:34-40.http://www.ncbi.nlm.nih.gov/htbinpost/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?c md=Retrieve&db=PubMed&list_uids=11845946&dopt=AbstractGoogle Scholar
- 14. Webster GF, Guenther L, Poulin YP. et al. A multicenter, double-blind, randomized comparison study of the efficacy and tolerability of once daily tazarotene 0.1% gel and adapalene 0.1% gel for the treatment of facial acne vulgaris. *Cutis*. 2002;69 (suppl2):4-11.http://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids= 12095066&dopt=AbstractGoogle Scholar

- 15. Leyden J, Lowe N, Kakita L, Draelos Z. Comparison of treatment of acne vulgaris with alternate-day applications of tazarotene 0.1% gel and once-daily applications of adapalene 0.1% gel: a randomized trial. *Cutis*.2001;67:10-16.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11499327&dopt=AbstractGoogle Scholar
- 16. Ellis CN, Millikan LE, Smith EB. et al. Comparison of adapalene 0.1% solution and tretinoin 0.025% gel in the topical treatment of acne vulgaris. *Br J Dermatol*.1998;139(suppl52):41-47.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9990420&dopt=AbstractGoogle Scholar
- 17. Graupe K, Cunliffe WJ, Gollnick HP, Zaumseil RP. Efficacy and safety of topical azelaic acid (20 percent cream): an overview of results from European clinical trials and experimental reports. *Cutis*.1996;57(suppl1):20-35.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8654128&dopt=AbstractGoogle Scholar
- 18. Becker LE, Bergstresser PR, Whiting DA. et al. Topical clindamycin therapy for acne vulgaris. *Arch Dermatol*. 1981;117:482-485.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6455095&dopt=AbstractGoogle Scholar
- 19. Dobson RL, Belknap BS. Topical erythromycin solution in acne. *J Am Acad Dermatol*.1980;3:478-482.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6452463&dopt=AbstractGoogle Scholar
- 20. Lesher JL, Chalker DK, Smith JG. et al. An evaluation of a 2% erythromycin ointment in the topical therapy of acne vulgaris. *J Am Acad Dermatol*.1985;12:526-531.http://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=3157709&dopt=AbstractGoogle Scholar
- 21. Jones L, Crumley AF. Topical erythromycin vs blank vehicle in a multiclinic acne study. *Arch Dermatol*. 1981;117:551-553.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6457568&dopt=AbstractGoogle Scholar
- 22. Habbema L, Koopmans B, Menke HE. et al. A 4% erythromycin and zinc combination (Zineryt) versus 2% erythromycin (Eryderm) in acne vulgaris: a randomized, double blind comparative study. *Br J Dermatol*. 1989;121:497-502.http://www.ncbi.nlm.nih.gov/htbin-

- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids= 2533878&dopt=AbstractGoogle Scholar
- 23. Leyden JL, Hickman JG, Jarratt MT. et al. The efficacy and safety of a combination benzoyl peroxide/clindamycin topical gel compared with benzoyl peroxide alone and a benzoyl peroxide/erythromycin combination product. *J Cutan Med Surg*.2001;5(1):37-42.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11281433&dopt=AbstractGoogle Scholar
- 24. Ellis CN, Leyden J, Katz HI. et al. Therapeutic studies with a new combination benzoyl peroxide/clindamycin topical gel in acne vulgaris. *Cutis*.2001;67(suppl 2):13-20.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11236210&dopt=AbstractGoogle Scholar
- 25. Lookingbill DP, Chalker DK, Lindholm JS. et al. Treatment of acne with a combination clindaymycin/benzoyl peroxide gel compared with clindamycin gel, benzoyl peroxide gel and vehicle gel: combined results of two double blind investigations. *J Am Acad Dermatol*.1997;37:590-595.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9344199&dopt=AbstractGoogle Scholar
- 26. Cunliffe WJ, Holland KT, Bojar R. et al. A randomized double-blind comparison of clindamycin phosphate/benzoyl peroxide gel formulation and a matching clindamycin gel with respect to microbiologic activity and clinical efficacy in the topical treatment of acne vulgaris. *Clin Ther*.2002;24:1117-1133.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids= 12182256&dopt=AbstractGoogle Scholar
- 27. Wolf Jr JE, Kaplan D, Kraus SJ. et al. Efficacy and tolerability of combined topical treatment of acne vulgaris with adapalene and clindamycin: a multicenter, randomized investigator blinded study. *J Am Acad Dermatol*.2003;49:S211-S217.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids= 12963897&dopt=AbstractGoogle Scholar
- 28. Richter JR, Bousema MT, De Boulle KLVM. et al. Efficacy of a fixed clindamycin phosphate 1.2%, tretinoin 0.025% gel formulation (Velac) in the topical control of facial acne lesions. *J Dermatol Treat*.1998;9:81-90.Google Scholar
- 29. Richter JR, Forstrom LR, Kiistala UO, Jung EG. Efficacy of the fixed 1.2% clindamycin phosphate, 0.025% tretinoin gel formulation (Velac) and a proprietary 0.025% tretinoin gel formulation (Aberela) in the World Journal of Pharmaceutical Science & Technology

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- topical control of facial acne. *J Eur Acad Dermatol Venereol*.1998;11:227-233.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9883434&dopt=AbstractGoogle Scholar
- 30. Rietschel RL, Duncan SH. Clindamycin phosphate used in combination with tretinoin in the treatment of acne. *Int J Dermatol*. 1983;22:41-43. http://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=6219964&dopt=AbstractGoogle Scholar
- 31. Mills Jr OH, Kligman AM. Treatment of acne vulgaris with topically applied erythromycin and tretinoin. *Acta Derm Venereol.*1978;58:555-557.http://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=83088&dopt=AbstractGoogle Scholar
- 32. Korting HC, Braun-Falco O. Efficacy and tolerability of combined topical treatment of acne vulgaris with tretinoin and erythromycin in general practice. *Drugs Exp Clin Res.* 1989;15:447-451.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids= 2534292&dopt=AbstractGoogle Scholar
- 33. Katsambas A, Graupe K, Stratigos J. Clinical studies of 20% azelaic acid cream in the treatment of acne vulgaris: comparison with vehicle and topical tretinoin. *Acta Derm Venereol Suppl* (*Stockh*).1989;143(suppl):35-39.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids= 2528257&dopt=AbstractGoogle Scholar
- 34. Hjorth N, Graupe K. Azelaic acid for the treatment of acne: a clinical comparison with oral tetracycline. *Acta Derm Venereol Suppl (Stockh)*. 1989;143(suppl):45-48.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids= 2528259&dopt=AbstractGoogle Scholar
- 35. Gollnick H, Cunliffe WJ, Berson D. et al. Management of acne: a report from a Global Alliance to Improve Outcomes in Acne. *J Am Acad Dermatol*.2003;49(suppl1):S1-S37.http://www.ncbi.nlm.nih.gov/htbin-
- post/Entrez/query?db=m&form=6&Dopt=r&uid=entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=12833004&dopt=AbstractGoogle Scholar