Effect of topical application of Nano retinol on mild to moderate acne vulgaris

Thesis

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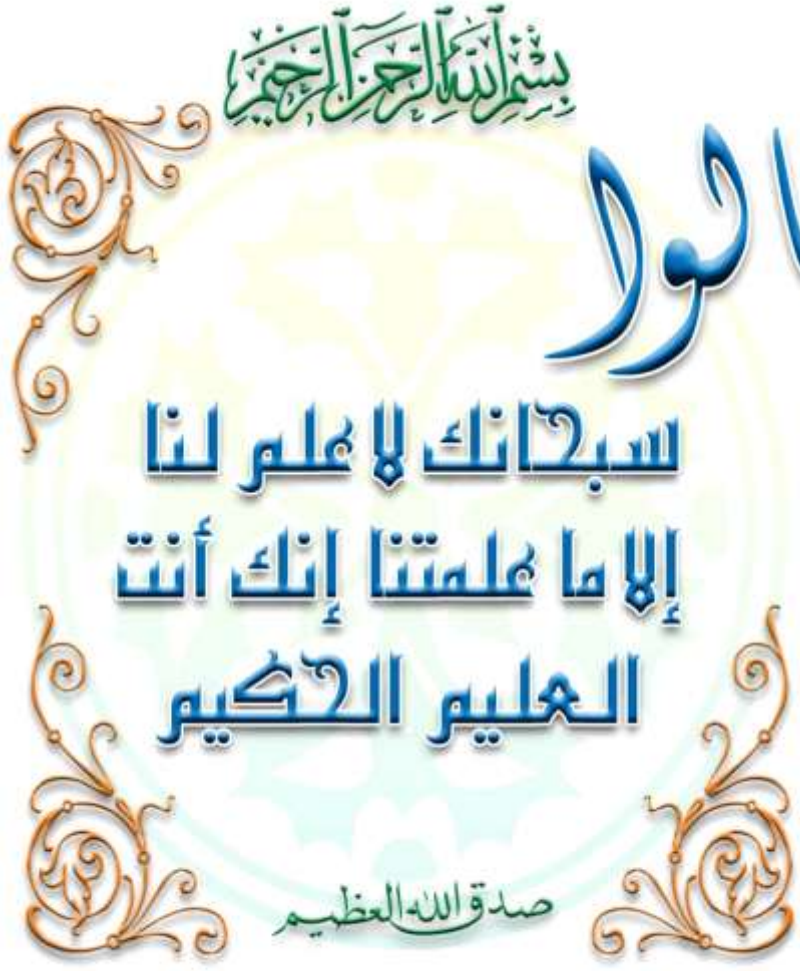

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Sally Sobhy Abd Elaziz

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List of Abbreviations

Abbr.	Full-term
atRA	**:** All-trans retinoic acid
C5a	**:** complement
CD1	**:** Cluster of differentiation
COC	**:** Combined oral contraceptive
CRH	**:** Corticotropin-releasing hormone
FDA	**:** Food and drug administration
G6PD	**:** Glucose-6-phosphate dehydrogenase
IL	**:** Interleukin
IPL	**:** Intensed pulsed light
LEDs	**:** Light emitting diode
MAL	: Methyl-aminolevulinic acid
NCs	**:** Nano capsule
NEs	**:** Nano emulsion
NLC	**:** Nano structured lipid carrier
nm	**:** Nanometer
P.acne	**:** Propionibacterium acne
PDT	**:** Photo dynamic therapy
PDT	**:** Photodynamic therapy
POD	**:** Podophyllotox
Sc	**:** Stratum corneum
SIS	**:** Skin immune system

SLN's : Solid lipid nanoparticles

SUV : Small unilamellar vesicles

TiO2 : Titanium dioxide

TLR2 : Toll like receptor 2

TNF alpha : Tumor necrosis factor

UVR : Ultra violet radiation

ZnO : Zinc oxide

5-ALA : 5-aminolevulinic acid

5α DHT : Dihydrotestosterone

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Abstract

Background: Acne vulgaris is a common skin condition with substantial cutaneous and psychologic disease burden. Estimates of acne prevalence vary substantially given the absence of a universally accepted or grading schema. **Aim of the Work:** The aim of work is to assess the efficacy and tolerability of topical application of Nano retinol in the treatment of mild to moderate facial acne vulgaris in comparison to classic retinoids. **Patients and Methods:** A prospective split face comparative clinical study include 30 female patients aged 15 to 27 years old participated for treatment of facial acne (24 with moderate acne and 6 with mild acne vulgaris). All patients recruited from outpatient clinic of dermatology department, Ain Shams University in the period from November 2015 to December 2016. History, clinical and dermatological examinations were done for each patient. **Results:** reduction in the total and inflammatory acne lesion count were reported to be significantly greater in the nano formulation as compared to the convential formulation .local adverse events were sigficantly less in the nano formulation as compared to the convential formulation. **Conclusion:** In the treatment of facial acne vulgaris Nanosomal retinol with iontophoresis is more efficacious and better tolerated than its conventional formulation with nearly no side effects and no precautions for use. **Recommendations:** More studies are needed on a wider scale, greater number of patients with different grades of acne vulgaris to support our findings.

Keywords: acne vulgaris, topical retinoids, Nano retinol.

Introduction

Acne vulgaris is a common inflammatory skin condition, although often perceived as a self-limited disease of adolescence, its prevalence remains high into adulthood. Nearly ninety percent of teenagers have acne vulgaris, and half of them continue to experience symptoms as adults **(Yeutzer et al., 2010).** By the age of forty years, one percent of men and five percent of women still have lesions **(Friedlander et al., 2011).**

While several different acne grading scales have been used in clinical trials, no standard method for acne grading has been adopted into practice. The basic acne severity index is proposed method for assessing acne severity based upon lesion type, number and location **(Bikowski, 2004).**

Acne vulgaris is categorized broadly into mild, moderate and severe forms. Lesions may persist on the face, chest or back areas with the greatest density of pilosebaceous unit **(Brown and Shaita, 1998).** Mild acne is typical limited to the face and is characterized by non-inflammatory closed and open comedones with few inflammatory lesions. An increasing number of inflammatory papule and pustule on face and often mild trunkal disease characterizes moderate acne. Finally, acne is considered severe when nodules and

cysts are present. In these cases, facial lesions are often accompanied by widespread trunkal disease **(Strauss et al., 2007).**

Acne vulgaris develops in the pilosebaceous unit that produces the comedones, this result from the interaction between numbers of factors: the abnormal development and differentiation of follicular cells of the pilosebaceous unit. The increased keratinization of follicular cells due to deposition of keratin within them, enhanced sebaceous activity with hyper seborrhea (oily skin), hyper colonization and growth of bacterium Propionibacterium acne within the follicles and inflammation and immunological reaction. Hyper cornification of the pilosebaceous duct results from the presence of androgens, local cytokines and abnormalities of the sebaceous lipids **(Kurokawa, 2009)**.

Guidelines in treatment of acne vulgaris focuses on acne severity and degree of inflammation. Treatment options include proper skin care, topical and oral antimicrobials, topical and systemic retinoids, benzoyl peroxide and oral contraceptives for female patients. These treatments may be used in combination to achieve disease resolution **(Haier and Shaw, 2004).**

Retinoids influence proliferation and differentiation of cells and reverse the abnormal desquamation by increasing

the follicular epithelial turn over and accelerating the shedding of corneocytes, which leads to an expulsion of mature comedones and suppression of micro comedone formation. The change of the follicular milieu of sebaceous gland apparatus by restoration of normal cornification promotes an inhospitable environment of Propionibacterium acne. Various in vivo and in vitro studies demonstrate also direct immunomodulatory activity of topical retinoids **(Wolf, 2002).**

The major adverse effects of topical retinoids are local skin irritation, including erythema, peeling, dryness, burning sensation and itching. Also, they can increase sensitivity of skin to ultraviolet light **(Yeutzer et al., 2009).**

Nanotechnology is a new branch of engineering consisting of the usage of Nano scale particles (100nm and smaller).Nano medicine is the application of Nano scale technology for diagnostic and therapeutic purposes in medicine. Nanotechnology applied to dermatology; represent one of most advanced fields for which increasing interest, both economic and scientific is rising **(Hia and Nasir, 2011)**

Applications of Nano medicine in dermatology include new direction in medical diagnosis, monitoring and treatment **(Hia and Nasir, 2011).** Retinoid compounds represent an example of positive applications of nanotechnology in drug

formulation. Retinoids are derived from vitA and are successfully used in the treatment of many dermatological conditions including acne vulgaris **(Souto and Muller, 2008).**

Major issue for retinoids therapy is local erythema, peeling, dryness and pain. Skin irritation side effects have been reduced by nanoparticle encapsulation **(Castro et al., 2009)**.

Improved stability and controlled release have been the primary focal points of Nano particle delivery for retinoids therapy **(Castro et al., 2009)**. A major advantage of such delivery system is the better tolerability of irritating retinoids, improving patient compliance as well as the avoidance of systemic side effects **(Jenning, 2000)**.

Aim of the Work

The aim of this work is to assess the efficacy and tolerability of topical application of Nano retinol in the treatment of mild to moderate facial acne vulgaris in comparison to classic retinoids.

Chapter 1
Acne Vulgaris

Definition:

Acne vulgaris is a common skin condition with substantial cutaneous and psychologic disease burden. Studies suggest that the emotional impact of acne is comparable to that experienced by patients with systemic diseases, like diabetes and epilepsy **(Uhlenhake et al., 2010).**

Epidemiology:

Acne is a highly common skin condition. Still, estimates of acne prevalence vary substantially given the absence of a universally accepted diagnostic or grading scheme. Additionally, estimates continue to change as the prevalence of acne decreases secondary to improved treatment modalities. Acne is most common in adolescents, affecting approximately 85% of teenagers **(Stathakis et al., 1997)**. It is typically thought as a disease of youth but, 12% of women and 3% of men will continue to have clinical acne until 44 years of age. It is well known that adult acne is more common in women. Adult acne typically represents chronic acne persisting from adolescence, not new-onset disease (**Gouldenn et al., 1999).**