

Formulation, Characterization and Evaluation of the Topical Nano-formula Gel to Treat Acne Vulgaris

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ABSTRACT

Acne and its harmful effects are considered reasons for the deterioration of the health, social, professional and psychological status of many people, especially in the age of sexual maturity and may lead to chronic skin abnormalities. The treatments used orally and parenterally cause hormonal disorders in addition to side effects on the digestive system. Topical treatment is one of the most important ways to treat acne and the skin abnormalities associated with it, which is characterized by lack of absorption through the skin, but modulating the local formula with nanotechnology and adding absorption stimuli increases the effectiveness of topical treatments. This study has advantage of designing and testing a new topical formula with standard kinetic and effective properties with the nano crystallization of spironolactone-ciprofloxacin-clindamycin-ascorbic acid to form the acne free formula to treat acne as no such design has been tested in laboratory studies. The study aims to increase the absorption, efficacy, and stability of topical treatment through the combination of nano crystalline crystals of spironolactone-ofloxacin-clindamycin-ascorbic acid and then test the resulting compound by diagnosing physical-chemical properties and measuring the absorptivity of the formula across the skin as well as measuring response and clinical safety. The study was conducted within three designs, which are laboratory, animal, and clinical. The laboratory study included diagnosing the physical and chemical properties of the formula by means of optical spectroscopy, pH measurement, peroxide, viscosity, and image processor technology in comparison to the traditional formula. The longitudinal and cross-sectional clinical study of the reviewers' registry included finding anti-inflammatory efficacy and assessing therapeutic safety. The random sample method and the statistical analysis of the results were adopted, the results showed that the acne free formula had the ideal physical properties as in Table 1 and the absorption is higher than the commercial formula and has stability for a period about 36 months. The rate of active substance absorption was 8% compared to 5% in the commercial formula. Also, the clinical safety parameters are better than their comparison. As in Figure 1 From the general results, there is a significant increase in absorptivity, efficacy, safety, and consistency of the formula acne-free compared to the commercial formula

Keywords: Acne treatment, Skin disorders, Topical therapy for acne vulgaris.

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INTRODUCTION

Acne is one of the common skin disorders in the age of sexual maturity for both males and females, with an estimated incidence of 30%.¹

Acne is characterized by the presence of microscopic pimples in the ducts of the sebaceous glands² and increased secretion of fatty acids and excessive response to male hormones.³ Also, these disorders are complicated by bacteria, and bacterial infections may be the cause, such as *Al-Kurani* bacteria and *Staphylococcus aureus*.⁴

And that the most important risks posed by acne are chronic skin abnormalities,⁵ which may afflict both sexes with social

frustration,⁶ which adds a cumulative burden to the economic situation.⁷ This is in addition to the side effects of medications used orally, such as hormonal disorders for anti-hormone therapy as well as the side effects of Antibiotics.⁸ Among the most important reasons that reduce the efficiency of common treatment include, reduced coefficient of vital abundance F As most antibiotics and hormones spread through the skin below the therapeutic level, which requires improvements in absorption,⁹ Reduced topical efficacy This is due to poor absorption through the skin, which in most formulas lacks absorption enhancers, in addition to the fact that many of the drugs produced are derivatives of specific efficacy.^{10,11}

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The effects of local irritation It is common to notice a skin reaction in the form of local irritation effects of the skin and sometimes a general sensitivity of the body to many topical acne formulations, which prevents continuous use by those in need and may increase the condition of skin infections.¹² The relative cost of a topical product ,Although some products are moderately priced, the need for them takes time, which creates a cumulative burden on personal income, as well as some expensive topical medications, but it forces many people to quit treatment.

All these reasons call for the development of modern nanotechnology of the topical formula to avoid side effects on the one hand, increase treatment efficiency and effectiveness, and reduce treatment costs on the other hand

MATERIALS

Spirolactone ; Sigma; (Taufkirchen, Germany); 1g filling powder, ofloxacin ; Panreac; Spain; 100 ml powder, retinol; Intatrad; Germany; 50 g oil Hydroxypropyl methylcellulose HPMC; Humilin; USA; 1 kg powder ascorbic acid ; Sigma Division; Svizzera-health care; 1 liter oil, diphenhydramine ; Intatrad; Germany; 1 liter oil, diphenhydramine ; Intatrad; Germany; 1 liter oil clindamycin ; Sigma-aldrich; Germany; 100 ml oil, tocopherol; Life reagents; Mumbai; 5 L liquid, glycerin ; Sigma Aldrich; Germany; 1 L liquid.

INSTRUMENTS

HPLC system; Conquer Scientific; California, USA; 5975C / 6890N, light microscope Zeits; Germany Staurt; UK; US151, mechanical stirrer Drucker diagnostic; USA; 642B; -centrifuge, Cecil; UK; CE 1021 ,UV/V spectrophotometer-UV sterilizer; Bio-Rad.com; Berkeley California.; Mini prepcell Alpha Brucker; Germany; 10066545-, Dialyzing catheter, dissecting set; Somatco; Carolina, USA.; 621485 BioLogics; USA; 150VT,- sonicator Seek-therma, computerized thermographic melting point analyzer; USA IOS Prime bioscience; Malaysia; Model APP 07, -Computerized pH meter USA, remote thermometer; Seek therma , Ball viscometer; India;

MODELS AND WORKING METHODS

- Study evaluating transdermal absorption of topical duct tape
- Study of the physical and chemical properties of formula acne free

Preparation Formula of Acne Free

Formula consists of two phases:

- Organic Phase
- Water Phase.

Prepare nanoparticles crystallization of spironolactone-ofloxacin-clindamycin-ascorbic acid) SOAC Crystallization.¹²

SOAC 95% is subjected with 5% to ultrafine grinding at a speed of ten thousand rpm at 25 ° C for one minute and then added to the mixture 70% ethyl alcohol after which the mixture is exposed to a temperature of 50°C until it dries under the

lyophilizer After drying, the mixture is taken to a compressor for 24 hours.^{13,14}

How to Prepare the Organic Phase

The SOAC nanoparticles are mixed with white paraffin at a rate of 20%. The first white paraffin is first heated to a temperature of 60°C while stirring quickly. Then, the pre-treated SOAC powder is added to super-grinding at a speed of 10,000 rpm for two minutes and is added to a liquid with calcine at a rate of 20% per minute with continuous mixing, then leave to cool to 20°C, with mixing continuing for five minutes.

How to Prepare the Water Phase

3 liters of water are heated to 45°C with continuous mechanical mixing at a speed of 100 rev / min. HPMC polymer (66% ratio and molar ratio 66%) is gradually added, the purity of the result from the impurity and conglomerate filtration of the polymer can be checked, and this is the result c.

The Method of Mixing the Aqueous Phase C with the Organic Phase b

Water phase C is moved with the same duration and speed at a temperature of 40°C in the mechanical mixer and then the organic phase B is added to it with stirring at the same speed until it cools to a temperature 20°C and this is the mixture d.

Pharmaceutical Characterization Tests

The Color of the Formula

The color can be measured in the in-kind method.¹⁵

The Odor

The odor is an important pharmacological characteristic of any product, because it is an indication of quality.¹⁶

Appearance

It is the physical description that appears to the eye.¹⁷

Homogeneity

It is tested to ensure consistency of appearance and if there are any substances collected in the gel after being settled inside the container.¹⁸

Viscosity¹⁹

Spreadability

Spreadability is evaluated on the expansion scale. Spreadability of formulas is calculated as

$$S = W \times L / T$$

Where S = scalability, W = tide weight to the top slide, L = the length of the glass slide, and T = the time it takes to separate the slide from each other Based on the results of 3 measurements.^{20,21}

pH

Measurement of pH in the water solutions of Acne Free gel, using a pH meter.²²

Rheology

The rheological property is determined to know the behavior of the gel flux.²³

Syneresis

Many gel systems undergo shrinkage when standing. The occurrence of synergy indicates that the original gel was dynamically unstable.²⁴

Grittiness

All microscopic gel formulations are evaluated for the presence of any concrete particles or under light microscopy.²⁵

Determine Extrudability^{26,27}

*Consistency also measured*²⁸

Pharmacokinetics and Absorption Kinetics Evaluation

Evaluate the Absorption of Active Substances

Where it is evaluated by the adhesive tape that contains a known concentration of the active substance and after an hour it is analyzed by the ultraviolet spectrum or by the HPLC device. Also, some methods of evaluation use the transdermal dialysis tubes and evaluate the result with the spectroscopy.^{29,30}

RESULT

Table 1: Results of General Pharmacokinetic Characteristics of AcneFree formula

<i>General pharmaceutical test</i>	<i>Result</i>	<i>Statistic</i>
1. Odor	Oderless	
2. AcneFree color	Pearl white	56% whiteness +/- 5%
3. Appearance	Opacity	40% opaque +/- 3%
4. Micibility	3 folds water micible	
5. Homogeneicity	Homogeneous sediment free	
6. Grittiness	No particles under the microscope	
7. Consistency	Emulsifying gel	
8. Swelling	No swelling after 3 months	
9. Aging	No aging before 18 months if cealed	
10. Thixotropy	20% flattening after 24 hours	
11. Dryness rate	12 days	
12. Dye absorption	Continuous phase appeared red amaranth	
13. Moisture absorption	No significant moisture absorption	
14. Rheology	Easily flow	
15. Structure	Gel plus emulsifying agent	

Table 2: Results of the pharmacokinetic properties of AcneFree topical formula

<i>Objective pharmaceutical tests</i>	<i>Result</i>	<i>Statistics</i>
1. Viscosity	119.2 cps Centipoise	1-/+
2. Density	1.008	0.001-/+
3. Spreadability	Score 1 easily spreadable	
4. Extrudability test	Score 3 good	
5. Microbial count	No microorganism per g	
6. PH value	6.7	0.1-/+
7. Acidity value	0.83	0.01-/+
8. Peroxide value	ME/1000g = 6	0.2-/+
9. Partition coefficient	30% hydrophobicity coefficient	
10. Solubility studies	Soluble in propylene glycol at 37C	
11. Conductivity	1A/V	0.1-/+
12. Saponification value	284	2-/+

Table 3: Results of the biological evaluation pharmacokinetics of the formula Acne

<i>The pharmacokinetic test</i>	<i>The results</i>	<i>Comment</i>
1. Animal skin penetration study by VCD	F = 10%± 1% with VCD	at 25c
2. Assessment of chicken skin absorption of active ingredients	F =7 % ± with patch absorption method	
3. AcneFree hydrophobicity determining	70%	

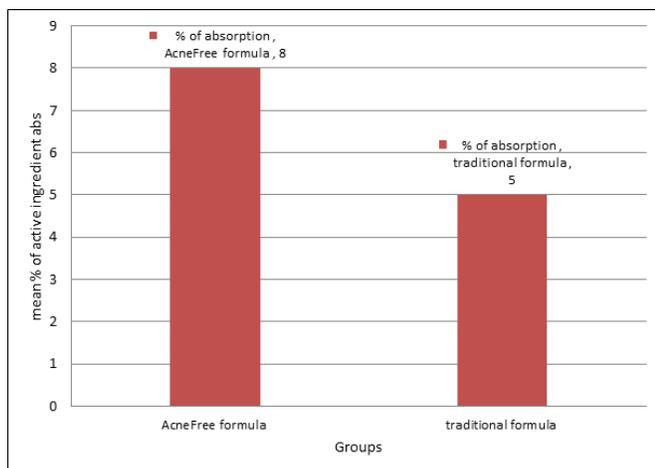


Figure 1: Percentage of the absorption evaluation of the vertical filtration cell of the animal's skin for the acne free formula compared with the commercial formula.

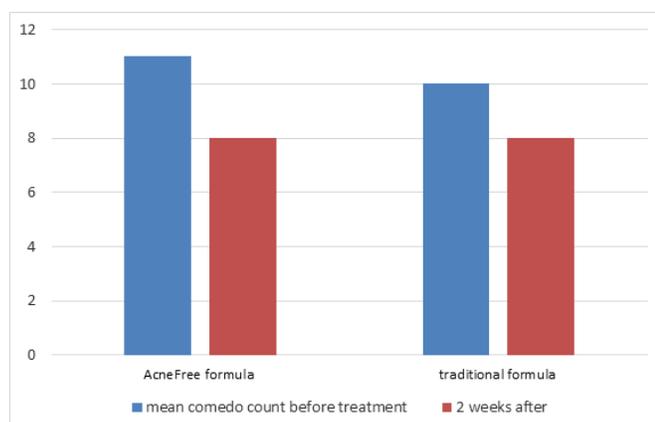


Figure 2: The number of acne blisters on the face as a response to daily treatment with Acne Free for two weeks compared to treatment with the traditional formula, where it is followed by a biometric device in the computer Image Analyzer

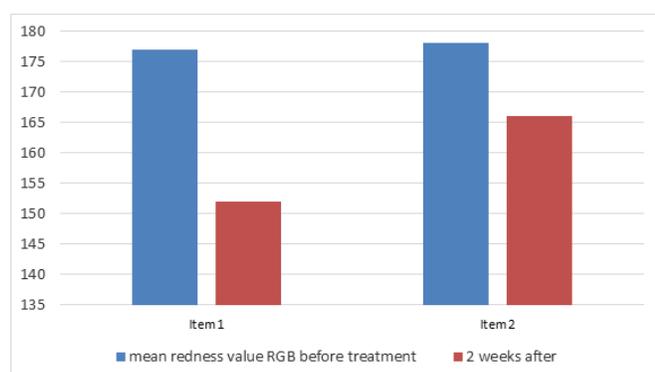


Figure 3: The rate of acne blisters in the face in millimeters +/- 0.2 mm in response to the daily treatment with Acne Free for two weeks compared to treatment with the traditional formula, where it is followed by a biometric device in the computer Image Analyzer

DISCUSSION

Acne vulgaris has a substantial impact on a patient's quality of life, affecting both self-esteem and psychosocial

development. Patients and physicians are faced with many over-the-counter and prescription acne treatments, and choosing the most effective therapy can be confusing³¹ there is a need for new formula for treatment of acne otherwise Topical products have the advantage of being applied to the affected area directly; thus decreasing systemic absorption and increasing the exposure of the pilo sebaceous units to the treatment. However, a major side effect of topically applied anti-acne products is skin irritation. Preparations for topical application are available as various formulations, including creams, gels, lotions, solutions and washes.³² In general, gel formulation is more preferred, among the other topical semisolid preparations, since it has long residence time on the skin, high viscosity, moisturizing effect on flaky skin due to their occlusive properties, more bio adhesiveness, less irritation, independent of water solubility of active ingredient, ease of application and better release characters.³³

Hence the topical gel formula that will be prepared contain effective ingredient like, Isotretinoin which affects all causative mechanisms of acne — it changes abnormal follicular keratinization, decreases sebum production by 70%, decreases *P. acnes* colonization and is anti-inflammatory³⁴ and Topical antibiotics ofloxacin, clindamycin that generally used for mild to moderate inflammatory acne. They have activity against *P. acnes*, and therefore act on the surface of the skin to reduce the stimulus for inflammation of the lesions (35in addition to Spironolactone is an alternative drug which can be used in the treatment of hormone related acne. Its mechanism is based on the fact that it is an androgen receptor blocker. It is especially effective for patients with inflammatory acne.^{35,36} This formulation was of high clarity, transparent, with Pearl white color, smooth homogeneous texture, and in good appearance and consistency. Values of the spreadability indicated that the gel formulations are easily spreadable., more than 90% of the contents were extrudable indicating they have excellent extrudability. There were no signs of microbial growth after incubation C for the sample gel compared with period of 24 hours at 37°C.

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