Full Length Research Paper

Dapsone in topical niosomes for treatment of acne vulgaris

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Acne vulgaris is a common inflammatory skin disorder. It affects the pilosebaceous units followed by an overgrowth by Propionibacterium acne bacteria. Dapsone is a sulfone antibiotic with an anti-inflammatory effect, which is considered to be accountable for its effectiveness in the treatment of acne vulgaris. The present study aims to prepare and evaluate the effectiveness of dapsone niosomes for topical application with an objective to control and prolong the release of the drug with improved skin penetration as a novel formulation for healing of mild to moderate acne vulgaris. Niosomes were formulated by thin film hydration method using different ratios of surfactants (various spans 20, 40, 60 and 80) and cholesterol and were investigated with respect to its shape, size, entrapment efficiency, Fourier transform infrared spectroscopy (FTIR) and in vitro release. Fifteen patients with mild to moderate acne vulgaris were selected and treated with dapsone niosomes as a single topical treatment for their acne lesions. Clinical assessment was done before and after 2 and 8 weeks of treatment. Niosomes containing span 60 showed a higher percentage of drug release after 24 h and greater entrapment efficiency as compared to other formulations. The clinical improvement was noticeable after 2 weeks of treatment with highly significant improvement of acne lesions after 8 weeks of treatment (P < 0.001). Dapsone niosomes is a promising topical formulation for safe, tolerable and effective drug delivery system with minimal side effects apart from mild erythema and post-inflammatory hyperpigmentation.

Key words: Dapsone, acne vulgaris, niosomes, topical, clinical application.

INTRODUCTION

Acne vulgaris is a multifactorial inflammatory skin disease commonly affecting adolescents and young adults with

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considerable physical, psychological, and psychosocial burden on those affected (Zaenglein et al., 2016). Acne is an increased sebum production due to the androgenic effect on the pilosebaceous unit leading to a chronic inflammatory disorder, microbial colonization by Propionibacterium acnes, changed keratinization and inflammation of hair follicles in various areas of the body including the forehead, cheek, chest, neck, and back (Williams et al., 2012). No typical therapy for acne, however, a proper medical course for improving lesions can be established for most patients. Convenient local applications of remedies including benzoyl peroxide, retinoids, and antibiotics when utilized in combination usually enhance management of mild to moderate acne (Williams et al., 2012). Dapsone, known as diaminodiphenyl sulfone, is an antibiotic routinely applied with rifampicin and clofazimine as a combination for leprosy therapy (Hiro and Hall, 2002). It has antimicrobial and anti-inflammatory effects in diseases which are characterized by the accumulation of neutrophils (Mancon et al., 2006; Abdelkader et al., 2014). Additionally, niosomes have been shown to increase the residence time of trapped substances in the epidermis while decreasing the availability of the drug in the systemic circulation which reduces the side effects (Marianacci et al., 2014). Incorporation of surfactants within niosomes may improve the efficiency of the drug, probably by promoting its uptake by the target cells. The most suitable surfactants for preparation of niosomes are those with alkyl chain length from C12–C18 (Mura et al., 2007; Nasr et al., 2008; Shilakari et al., 2013; Sharma et al., 2015). Niosomes can be prepared by hydration of synthetic nonionic surfactants either with or without cholesterol. The presence of the steroidal molecule (cholesterol) enhances the solidity of the bilayer and its presence in the cell membrane as an important ingredient affects the bilayer fluidity and permeability. The present study was aimed at the formulation and evaluation of dapsone-loaded niosomes for topical application with an objective to control and prolong the release of the drug with improved skin penetration for treatment of acne. Niosomes (empty and drug loaded) were formulated by utilizing various ratios of surfactant (different span grades 20, 40, 60 and 80) and cholesterol by thin film hydration technique. The in vitro properties of the prepared niosomal formulations and their clinical usefulness for treatment of acne vulgaris were evaluated.

MATERIALS AND METHODS

Dapsone was gifted by El-Nile Co., El-Sawah square-America - Cairo, Egypt; sorbitan monolaureate (span 20); sorbitan monopalmitate (span 40); sorbitan monostearate (span 60); sorbitan monooleate (span 80) and cholesterol were purchased from Sigma-Aldrich chemical Co. St. Louis MO (USA) Chloroform, methanol and other chemicals were of analytical grade.

Preparation of niosomal formulation

In the present study, niosomal formulations of dapsone were prepared by thin film hydration technique as reported earlier with slight modifications (Balakrishnan et al., 2009) by using 5 mg of dapsone and a specified amount (300 mmol) of lipids (surfactant: cholesterol) at molar ratio of 9:1, 8:2, 7:3, 6:4, 1:1 and utilizing different grades of spans (span 20, span 40, span 60 and span 80) (Table 1). Accurately weighed quantities of surfactants and cholesterol were taken to give the desired ratio and were dissolved in 10 mL of 2:1 v/v chloroform/methanol mixture in a round bottom flask. Then, accurately weighed amount of drug was added to the solvent. The solvent was evaporated in a rotary evaporator (Stuart RE300). Germany under a vacuum of 20 inches of Hg at a temperature of 60°C at 150 rpm until a smooth, dry lipid film was obtained followed by introducing under high vacuum through
Table 1. Composition of the prepared dapsone niosomal formulations using various grades of non-ionic surfactants (spans) with different molar ratios of surfactant to cholesterol and the calculated total lipid weight in all formulae.

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Molar ratio</th>
<th>Surfactant (g/mol) Mwt:346.00</th>
<th>Cholesterol g/mol Mwt: 386.65</th>
<th>Total lipid weight (mg)</th>
<th>Equivalent no. of moles (mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>span 20</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FA1</td>
<td>1:1</td>
<td>52.00</td>
<td>58.00</td>
<td>110.00</td>
<td>300</td>
</tr>
<tr>
<td>FA2</td>
<td>6:4</td>
<td>62.28</td>
<td>46.40</td>
<td>108.68</td>
<td>300</td>
</tr>
<tr>
<td>FA3</td>
<td>7:3</td>
<td>72.66</td>
<td>35.00</td>
<td>107.46</td>
<td>300</td>
</tr>
<tr>
<td>FA4</td>
<td>8:2</td>
<td>83.55</td>
<td>23.20</td>
<td>106.20</td>
<td>300</td>
</tr>
<tr>
<td>FA5</td>
<td>9:1</td>
<td>93.42</td>
<td>11.60</td>
<td>105.02</td>
<td>300</td>
</tr>
<tr>
<td>span 40</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FB1</td>
<td>1:1</td>
<td>60.45</td>
<td>58.00</td>
<td>118.45</td>
<td>300</td>
</tr>
<tr>
<td>FB2</td>
<td>6:4</td>
<td>72.54</td>
<td>46.40</td>
<td>118.94</td>
<td>300</td>
</tr>
<tr>
<td>FB3</td>
<td>7:3</td>
<td>84.63</td>
<td>35.00</td>
<td>119.43</td>
<td>300</td>
</tr>
<tr>
<td>FB4</td>
<td>8:2</td>
<td>96.72</td>
<td>23.20</td>
<td>119.92</td>
<td>300</td>
</tr>
<tr>
<td>FB5</td>
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<td>108.81</td>
<td>11.60</td>
<td>120.41</td>
<td>300</td>
</tr>
<tr>
<td>span 60</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>1:1</td>
<td>64.65</td>
<td>58.00</td>
<td>122.65</td>
<td>300</td>
</tr>
<tr>
<td>FC2</td>
<td>6:4</td>
<td>77.58</td>
<td>46.40</td>
<td>123.98</td>
<td>300</td>
</tr>
<tr>
<td>FC3</td>
<td>7:3</td>
<td>90.50</td>
<td>35.00</td>
<td>125.50</td>
<td>300</td>
</tr>
<tr>
<td>FC4</td>
<td>8:2</td>
<td>103.44</td>
<td>23.20</td>
<td>126.64</td>
<td>300</td>
</tr>
<tr>
<td>FC5</td>
<td>9:1</td>
<td>116.57</td>
<td>11.60</td>
<td>127.97</td>
<td>300</td>
</tr>
<tr>
<td>span 80</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FD1</td>
<td>1:1</td>
<td>64.35</td>
<td>58.00</td>
<td>122.35</td>
<td>300</td>
</tr>
<tr>
<td>FD2</td>
<td>6:4</td>
<td>77.22</td>
<td>46.40</td>
<td>123.62</td>
<td>300</td>
</tr>
<tr>
<td>FD3</td>
<td>7:3</td>
<td>90.10</td>
<td>35.00</td>
<td>125.10</td>
<td>300</td>
</tr>
<tr>
<td>FD4</td>
<td>8:2</td>
<td>102.96</td>
<td>23.20</td>
<td>126.16</td>
<td>300</td>
</tr>
<tr>
<td>FD5</td>
<td>9:1</td>
<td>115.83</td>
<td>11.60</td>
<td>127.43</td>
<td>300</td>
</tr>
</tbody>
</table>

Vacuum pump for at least three hours for removal of residual content of chloroform. Furthermore, the flask was kept in vacuum desiccators overnight for complete removal of chloroform (Mukherjee et al., 2007). Then, the film was hydrated with 10 mL of PBS pH 7.4 for 1 h at 60°C with shaking on a water bath. The niosomal suspension was retained at 2 to 8°C for 24 h.

Evaluation of niosomal formulation

Developed niosomal formulations were evaluated with respect to particle size, shape, entrapment efficiency, FT-IR and in vitro drug release profile.

Entrapment efficiency

Entrapment efficiencies of niosomal formulations were determined by centrifugation method. For this, 1 mL niosomal suspension was poured into a centrifugation tube and centrifuged by using cooling centrifuged (REMI cooling centrifuge) at 15000 rpm at 4°C for 10 min. The clear fraction was further used for the determination of free drug by using UV/visible spectrophotometer at 298 nm. The entrapment efficiency was calculated using the following formula:

\[
\text{Entrapment efficiency (EE%) = } \frac{(A_t - A_f)}{A_t} \times 100
\]

Where \(A_t\) is the concentration of total drug and \(A_f\) is the concentration of the free un-entrapped drug.

Particle shape and morphology

Shape and morphology of selected empty niosomal formulations and drug-loaded niosomal formulations prepared using span 60 were determined by scanning electron microscope with different magnifications.

Particle size measurement

The mean particle sizes and zeta potentials of selected niosomal formulations prepared from different grades of spans with the same ratio (FA2, FB2, FC2 and FD2) were analyzed by dynamic light scattering using a Zetasizer Nano ZS (Malvern Instruments, UK) at 25°C. The analysis was carried out after proper dilution in 1:100 deionized water to the concentration appropriate for measurement. The results are shown in Table 2.
Fourier transform infrared spectroscopy (FT-IR) studies

FT-IR studies were performed to detect the interaction between the drug dapsone, the utilized non-ionic surfactant, and cholesterol. FT-IR spectra were carried out using FT-IR Spectrometer® (Perkin Elmer Instruments) by the potassium bromide (KBr) pellet technique. Samples were blended with KBr powder and pressed to form discs by a torque wrench. Each disc was scanned over the range wavelength 400 to 4000 cm⁻¹. The FT-IR spectra of the selected niosomal formula (FC2) with its components, the raw dapsone, span 60 and cholesterol are displayed in Figure 3.

In vitro drug release

Dapsone release profile from niosomal formulations was determined using the dialysis method. An accurately measured volume of dapsone niosomal formulation equivalent to 0.3 mg/mL transferred to an open-ended glass cylinder (10 cm length and 2.5 cm diameter) and that was sealed at its lower end with presoaked cellulose membrane as dialyzing membrane fitted by elastic ends. The glass cylinder was suspended in a beaker containing 50 mL phosphate buffer (pH 6.8) and was kept at 37±1°C and stirred continuously at 50 rpm using magnetic stirrer. The receptor compartment has been replaced by fresh PBS immediately at the predetermined time intervals, 2 mL aliquots were withdrawn from each cylinder and replaced with the same volume of fresh PBS that was kept at the same temperature. The drug content was determined spectrophotometrically at λmax 298 nm. The % cumulative drug release vs time was plotted and shown in Figure 4.

Patient study

The present study was conducted on 15 patients suffering from mild to moderate acne vulgaris according to the global acne grading score system (Adityan et al., 2009). Patients were recruited from attendants of the Dermatology Outpatient Clinic, Minia University Hospital. The duration of scars ranged from 1 to 14 years with a mean of 6.63 ± 4.03. Patients enrolled in the study did not receive any treatment for their acne lesions at least 3 months before the study. An informed consent was taken from each volunteer for treatment, photography and clinical follow-up. This study was approved by the Committee for Postgraduate Studies and Research of Faculty of Medicine, Minia University. All volunteers have been subjected to full history taking, general and local examination and photographing of the lesions. Exclusion criteria included pregnancy, lactation, presence of any skin condition that would interfere with the diagnosis or assessment of acne vulgaris, history of hypersensitivity or allergy to dapsone, or methemoglobinemia or subjects with known G6PD (Glucose 6-Phosphate Dehydrogenase) deficiency or congenital or idiopathic methemoglobinemia. Dapsone niosomes were applied as a topical treatment for acne lesions every night for 8 weeks as a thin film over the acne lesions. Clinical evaluation according to the global acne grading system as well as any side effects were reported before, 2 and 8 weeks after treatment.

Statistical evaluation

The collected data had been analyzed and figured using a computer-based program, SPSS software package for statistical analysis (SPSS for Windows, Version 16.0, copyright © SPSS Inc., Chicago, IL, USA). The data had been summarized in the form of mean ± SD. The significance of clinical improvement in the same group was assessed using Dependent (paired) T-test. This was interpreted in the form of P value. The value of *P ≤ 0.05 was regarded statistically significant.

RESULTS AND DISCUSSION

Entrapment efficiency percentage (EE%)

Entrapment efficiency of the drug-loaded niosomal formulation was found to be increased with increasing the cholesterol ratio from 10 to 50% whereas entrapment efficiency decreases on further increase in cholesterol ratio from 1 to 1.5 (Figure 2). This might be due to two aspects: First, with increase cholesterol ratio, hydrophobicity, and stability of bilayers vesicles increase and permeability decrease which may causes an effective entrapping of the hydrophobic drug into the bilayers during formation of vesicles. Second, a larger amount of cholesterol may act competitively with the drug for the packing area inside the bilayer thus preventing the drug as the surfactants assembled. Furthermore, comparing the various niosomal formulations containing different grades of spans (span 20, span 40, span 60 and span 80) at different ratios of surfactant to cholesterol, span 60 containing niosomal formulation (FC2) displayed the highest entrapment efficiency as compared to other formulations. This might be due to the fact that span 60 has longest alkyl chain length compared to other span series (Asthana et al., 2016). Briefly, entrapment efficiency of all niosomal formulations with different grades of spans was found in the following order: Span 60 > span 40 > span 80 > span 20.

Table 2. Particle sizes and zeta potentials of selected dapsone-loaded niosomal formulations FA2, span 20 (6:4); FB2, span 40 (6:4); FC2, span 60 (6:4) and FD2, span 80 (6:4).

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Zeta potential (mV)</th>
<th>Particle size (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FA2</td>
<td>-11.67</td>
<td>6.32</td>
</tr>
<tr>
<td>FB2</td>
<td>-18.34</td>
<td>4.80</td>
</tr>
<tr>
<td>FC2</td>
<td>-29.97</td>
<td>2.47</td>
</tr>
<tr>
<td>FD2</td>
<td>-22.11</td>
<td>2.25</td>
</tr>
</tbody>
</table>
Particle shape and morphology

Shape and morphology of niosomal formulations were determined by scanning electron microscopy. It was clearly observed that niosomal vesicles FC1 and FC2 are rounded and symmetrical with a smooth surface and the niosomes were in micrometer size range (Figure 1A). Similarly, the drug-loaded niosomes of the same formulations were almost spherical in shape with larger particle size than the empty ones (Figure 1B). However, some aggregations and curds were displayed in case of FC3 and FC4 niosomal formulation.

Particle size

The particle size of the niosomal formulations prepared using different grades of spans was determined by optical microscopy (OPTEC 097876). It was clearly observed that the particle sizes of niosomes decreased consistently.
Figure 2. Entrapment efficiency of niosomes containing different grades of spans at various ratios.

from span 20 to span 80 and are found in the following order: Span 20 > span 40 > span 60 > span 80. The particle sizes of empty niosomal formulations were reported in the range of 3.89 to 8.32 μm. This might be due to the increase in the hydrophobicity of the surfactant from span 20 to span 80. The decrease in surface free energy with increasing the hydrophobicity of surfactants may be the major attribute of reduction in the particle size of niosomes. A similar pattern in particle size was observed in case of drug loaded niosomal formulations as previously discussed (Sambhakar et al., 2011). Mean particles’ size of drug loaded niosomes was found to be greater than the unloaded niosomes at each ratio of drug: cholesterol: surfactant with different grade of spans (20, 40, 60 and 80). Based on the results, FC2 niosomal formulation was chosen for measuring of zeta potential using Zetasizer. Zeta potential of FC2 was -29.97 mV which indicates good stability of the selected formulation.

**FT-IR studies**

Among the reported amphiphilic molecules, spans was used to investigate the encapsulation of dapsone for topical delivery in treatment of acne. FT-IR studies were performed in order to assure the compatibility between the drug, cholesterol and the utilized surfactant which gave the highest EE% (span 60). Niosomes are self-assembled of spans (amphiphiles) in aqueous media resulting in closed bilayer framework. It was reported that construction of niosomes is rarely extemporaneous and includes some kind of energy such as physical stirring or heating (Sharma et al., 2015). The FT-IR spectra of pure dapsone, span 60, cholesterol, and dapsone-loaded niosomes (FC2) were shown in Figure 3. It can be observed that a band at 3300 to 3400 cm⁻¹ corresponding to the stretch of the amine group (N-H), and peaks corresponding to the bending vibration of -NH₂ groups between 1590 and 1550 cm⁻¹. The bands at 1143 and 1180 cm⁻¹ are ascribed to the symmetric and asymmetric vibrations of the sulfone group (-SO₂). The IR spectrum of cholesterol displays two characteristic peaks in the region between 2800 and 3200 cm⁻¹, which are corresponding to C-H stretching vibrations of methyl groups and vibrations of cyclic hydrocarbons. All the previous bands are clearly observed in the spectrum of niosomal formulation at the same wave numbers. It was revealed that there was no major shifting as well as any loss of functional peaks between the spectra of drug, cholesterol, span 60 and dapsone-loaded niosomes. It
suggests that the formulation components; span 60, cholesterol and dapsone do not interact to form any additional chemical entity but remain as mixture (Chatwal and Anand, 2002).

**In vitro drug release**

*In vitro* studies of selected formulations were carried out in PBS pH 6.8 by dialysis technique (Sathali and Rajalakshmi, 2010) on a magnetic stirrer. It was clearly observed from the data as shown in Figure 4 that *in vitro* drug release of niosomes containing span of different series (60 and 80) was sharply increased up to 24 h. Maximum drug release, that is, 96.78%, was reported in case of niosomes containing span 60 as compared to other series of span 80 after 24 h. The observed increase of *in vitro* release of span 60 formulation might be due to the longest alkyl chain length of span 60 and thus possesses highest release profile (Sambhakar et al., 2011). In contrast, span 80 has monounsaturated alkyl chain and thus has lowest release profile compared to span 60.

**Patient study**

The study included 15 patients with acne vulgaris. Nine patients had mild acne lesions (60%), while the remaining 6 patients had moderate acne (40%). Twelve patients were females (80%) and 3 were males (20%), their age ranged from 15 to 25 years with a mean age ± SD of 19.53 ± 3.04 years. The duration of acne ranged from half to 4 years with a mean duration of 1.53 ± 0.92. Inflammatory lesions (papules and pustules) were present in 8 patients (53%), meanwhile, non-inflammatory lesions (comedones) were the main lesions in 7 (47%) of patients. Before treatment, the clinical evaluation revealed a score ranged from 6 to 28 with a mean score of 15.53 ± 6.8. Clinical improvement was noticeable after 2 weeks of treatment with a highly significant decrease of the score to 9.13 ± 3.99 (P <0.001). With continuing treatment up to 8 weeks, the clinical improvement still showed the highly significant decrease of the score with a mean of 7 ± 3.49 when compared to before treatment (P <0.001). Also, a highly significant improvement was observed when comparing mean scores of lesions after 2 and 8 weeks of treatment (P = 0.001) (Figure 5A).
The effect of dapsone niosomal topical application was clear on both non-inflammatory and inflammatory acne vulgaris during the whole duration of the study. In non-inflammatory, there was a highly significant decrease in the severity of lesions from 9.57 ± 2.15 before treatment to 5.86 ± 2.67 (P = 0.001) and 4.29 ± 2.63 (P = 0.001) after 2 and 8 weeks of treatment, respectively. There was a non-significant difference when comparing lesion after 2 and 8 weeks (P = 0.06) (Figure 5B).

Meanwhile, inflammatory acne lesions showed a highly significant decrease in the severity of lesions from 20.75 ± 4.68 before treatment to 12 ± 2.39 (P < 0.001) and 9.38 ± 2.13 (P = 0.001) after 2 and 8 weeks of treatment, respectively. There was a significant difference when comparing lesion after 2 and 8 weeks (P = 0.009) (Figure 5C). Side effects were minimal apart from mild erythema in 2 patients (13%), which resolved after one week of treatment. Post-inflammatory hyperpigmentation was reported in one case (6.5%) (Figure 5D).

Previous data suggested that the topical dapsone 5% gel showed good efficacy for the alleviation of inflammatory and non-inflammatory acne lesions with no hematological side effects accompanied with oral dapsone (Stotland et al., 2009; Kircik, 2010). In the present study, a novel formulation was introduced for dapsone as niosomes which allowed good penetration and absorption of active material with lower risk of either local irritation or systemic absorption. The once-daily topical application of dapsone demonstrated very promising results with obvious clinical improvement as early as 2 weeks of initiation of treatment, which is maintained with better response up to 8 weeks (P < 0.001). Also, a highly significant improvement was observed when comparing the mean scores of lesions after 2 and 8 weeks of treatment (P < 0.001). Despite the fact that topical therapy is preferable by both acne patients and the physicians, no topical mediation has essentially provided an anti-inflammatory action (Kircik, 2010). Both inflammatory and non-inflammatory lesions of acne vulgaris responds well to dapsone niosomal topical application with more pronounced effect on the mean score of inflammatory lesions (P < 0.001). The obtained results were in agreement with previous study (Al-Salama and Deeks, 2017) which reported a reduction in acne severity (as per the Global Acne Assessment Score) and lesion counts with once-daily dapsone 7.5% versus vehicle. The advantages of using dapsone 7.5% gel over vehicle were observed as early as the second week for inflammatory lesion counts, and from the fourth week or the eighth week for other results. In the present study, side effects were minimal apart from mild erythema in 2 patients, which resolved after one week of treatment. Post-inflammatory hyperpigmentation was also reported in one case. Post-inflammatory hyperpigmentation is a recurrent problematic issue and may represent the consequence of many cutaneous

**Figure 4.** Comparative in vitro release profile of selected dapsone-loaded niosomal formulations in phosphate buffer pH 6.8 at 37±1°C.
diseases as well as therapeutic medications resulted from hypersensitivity responses especially with dark skin populations (Chang, 2009). These results reflect the safety and tolerability of the dapsone niosomes when compared with dapsone gel 7.5% which showed adverse effects of mild to moderate severity as stinging/burning, dryness, scaling, and erythema (Thiboutot et al., 2016). In a previous study, dapsone niosomal gel was studied for its efficiency in treatment of cutaneous leishmaniasis (Aflatoonian et al., 2016). They found it as a promising alternative therapy for oral treatment with fewer side effects. However, they did not report any results for physicochemical characteristics of the prepared niosomes including particle size analysis, encapsulation efficiency or in vitro release study. Also, dapsone was incorporated into nanoemulsion which promoted its permeation through the skin (Borges et al., 2013). Nevertheless, to the best of the authors knowledge, there are no reports in the literature discussing the effect of dapsone niosomes on acne vulgaris.

Conclusion

The main focus of this study was the formulation and evaluation of dapsone niosomes for clinical behavior. Niosomal formulae (empty and drug loaded) were prepared by utilizing various ratios of surfactant (different span grades 20, 40, 60, and 80) and cholesterol by thin film hydration method and were investigated for their in vitro characteristics including particle size, shape, FT-IR, EE% and in vitro release pattern. Span 60 containing niosomal formulation (FC2) showed the highest entrapment efficiency with satisfied spherically shaped particles and a size of 3.65 μm. Moreover, FC2 showed the highest percentage of prolonged drug release over 24 h as compared to other formulae. This study revealed that niosomal preparations provide sustained and prolonged delivery of drug with enhanced clinical usefulness. It highlights the effect of dapsone niosomes as a topical once-daily treatment of mild to moderate acne vulgaris with early and maintained clinical improvement.
together with minimal side effects. The authors are aware that one of the limitations of the present study is relatively the small number of patients and the cost of niosome preparation. Hence, further studies on a larger group of patients are needed to confirm and clarify such findings.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

REFERENCES


