Formulation and in vitro Evaluation of Dapsone Topical Gel 5%

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Abstract

Introduction: Dapsone gel (5%) is found to be effective in treating acne. The study was to develop a topical formulation of dapsone in Iran.

Objective: Determination of appropriate formulation for generic form of this drug in the treatment of acne.

Materials and Methods: Samples of the base of gel were made in the range of 0.3%-5% by dissolving Carbomer 934P in distilled water, and their physical properties and pH were evaluated. Then, Dapsone was dissolved in its appropriate solvent, diethylene glycol monoethyl ether (DEG) and were introduced into gel base. Afterwards, using Design Expert software 13 samples and in the next step 17 samples were designed, made and their rheological properties and pH were evaluated. Then, two formulations were selected and were characterized by drug content, physicochemical properties, rheology and stability and found to be in accordance with the US Pharmacopeia.

Results: The gel bases containing carbomer in the range of 1-3% were appropriate. The pH value of gel bases in first 13 samples were between 5-7 and the viscosity range between 16530-2980000(cp). The viscosity of range of 17 designed samples was between 1100-760000(cp). The final sample with 1% carbomer content had the viscosity range of 14075-268000(cp) and drug release of 78/1% after 3 hours. The sample with 2% carbomer content had the viscosity range of 92660-557000(cp) and drug release of 76% after 3 hours.

Conclusion: Viscosity and drug release of both samples were in accordance with pharmacopeia. However, the sample containing 1% carbomer is more commercially suitable and more appropriate lowering pH of the skin.
Conflict of interest: non declared

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Extended Abstract

Introduction: In 2000, a topical formulation of dapsone (Aczone 5%) was developed in Canada. Dapsone gel (5%) is found to be effective in treating acne. However, it is not available in Iran and limited number of studies have addressed it. Acne is a common problem in Iran, and it is important to introduce new and effective products, such as the Dopson gel, in the Iranian society, which comprises a large percentage of the young population. Presentation of the generic Dopson gel requires a great deal of research into the formulation and its compliance with world standards and clinical trials to observe its efficacy in patients.

Objective: The aim of this study was to develop a topical formulation of dapsone in Iran to be effective against acne vulgaris.

Materials and Methods: Dapsone powder (Batch No: 8.21073.0250), sodium hydroxide and Diethylene glycol (Batch No: 8.03127.2500) were purchased from Merck, Germany, and Carbomer powder 934P used by Corel Pharm Chem India (donated by Behvazan Pharmaceutical Company) (Batch No: 22013015). Devices used in this study were Brookfield DV1 viscometer for viscosity measurement, dissolution testing machine Pharmatest model PTWS D610, Spectrophotometer Cecil Model CE 7250 and Proline Model B210 pH meter.

To prepare the 5% Dapsone gel, the gel base was prepared first. Carbomer gel was used to prepare the gel base. In a certain volume of distilled water, the carbomer was gradually added to the desired concentration. Accordingly, different percentages of gel were prepared to obtain the appropriate concentration of the gel. The common percentage of carbomer gel making material is between 0.5 and 2%. Sampling was done with 0.3% of distilled water. After adding the final solution for 24 hours, it was placed at room temperature till the carbomer powder completely dissolved and the obtained gel was uniform without bubbles. The obtained gel had a pH of 3 to 4.in order to increase the pH of the solution, NaOH was used. It was gradually added to the solution and stirred completely. After a few minutes, the pH of the solution was measured. Then, using Design Expert software, 13 samples were designed, made and their rheological properties and pH were evaluated. Dapsone was dissolved in its appropriate solvent, then diethylene glycol monoethyl ether (DEG) was introduced in gel base. Again 17 samples were designed and evaluated. Then, two formulations were selected is in accordance with the US pharmacopeia and the two formulations were characterized by drug content, physicochemical properties, rheology and stability as the US Pharmacopeia.

Results: to make the gel base, the appropriate concentration range for the gel base was 3.5% -1%. At a low concentration of 1% gel it was relatively dilute, however, the gel was formed. At high concentration, the 3.5% carbomer was relatively firm from the beginning, therefore, it required a high degree NaOH to adjust the pH. At this stage, 17 samples were obtained and NaOH added to the optimum pH. Thus, each time the gel was prepared, its pH was also raised to 6. The appearance of the gel was clear, transparent and free of bubbles. Suitable pH range and appropriate range of carbomer percentage were 7-5 and 1%-3.5% respectively. UV-Vis spectrometry was used to make Dapsone standard curve. The R^2 regression coefficient was 0.999 and the intercept was 0.008 that indicates the accuracy of the standard curve. Results for the measurement of Dapsone gel viscosity and gel base showed that after preparation of 13 formulations, sample 13 had the lowest viscosity of 16530 (CP) due to its low carbohydrate content (0.5%) and lowest pH (pH = 5). And sample 12 had the highest viscosity of 2980000 (CP) due to the highest carbomer content (3.27) and pH of 6. With the experimental design program and considering the three factors that influence the final gel, the amount of carbomer, pH and solvent, again 17 experimental samples were designed by CCD method. The lowest viscosity 1100 (cp) was observed in the sample 17 with the lowest carbohydrate content (0.3%), compared to samples 5 and 15 which had similar carbomer content but have more solvent support. It can be concluded that the solvent support has reduced the viscosity of the formulation. In contrast, sample 9 with the highest amount of carbomer (3%) had the highest viscosity 760000 (cp). Samples 7 and 15 became two-phased during preparation, therefore, the corresponding values are not entered in the calculations. The viscosity of range of 17 designed samples was between 1100 -760000(cp). The final sample with 1% carbomer content had the viscosity range of 14075-268000(cp) and drug release of 78/1% after 3 hours and the sample with 2% carbomer content had the viscosity range of 92660-557000(cp) and drug release of 76% after 3 hours.

Conclusion: After making 17 test samples of the final gel and measuring their pH and viscosity, two samples were selected as suitable samples that contained1% and 2% carbomer and pH 5 – 6.5. The first sample containing 1% carbomer, with less amount of carbomer, is commercially more convenient and since most of acne patients have oily skin, the 1% sample is more appropriate in lowering the pH of skin. Viscosity

and drug release of both samples were in accordance with US pharmacopeia. The release rate was measured at different minutes for both samples and the result was a suitable release. More than 70% of the target dose was released after three hours so that sample 1, with a release of more than 86.1%, was found to be more suitable.

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