WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 5, 139-147. Research Article ISSN 2277– 7105

THE DEVELOPMENT OF DIFFERENT FORMULATIONS CONTAINING 2% CHLORHEXIDINE DIGLUCONATE AND PRELIMINARY EVALUATION OF THE STABILITY OF THE FORMULATIONS.

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Article Received on
06 March 2016,
Revised on 26 March 2016,
Accepted on 15 April 2016
DOI: 10.20959/wjpr20165-6128

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ABSTRACT

Hand washing using soap for degerming is essential to reduce the risk of infection, and it is preferable to use antiseptic liquid soaps. A chlorhexidine digluconate solution at low concentrations acts as a bacteriostatic agent, and as a bactericidal agent at higher concentrations. This study aimed to analyze different liquid soap formulations containing 2% chlorhexidine gluconate and analyze which of the formulations has adequate stability. Twelve formulations were produced containing chlorhexidine with different concentrations of hydroxyethylcellulose and citric acid. After preparation, the samples were submitted to centrifugation and a thermal stress test and analyzed for the presence of signs of instability. Of the twelve samples analyzed, eleven showed signs of instability in both tests. Only the formulation containing 1% hydroxyethylcellulose and 0.5% citric acid showed adequate stability. The preliminary stability study led to the selection of the best formulation for the development of liquid soap containing 2% chlorhexidine

digluconate, and this was the formulation with 1% hydroxyethylcellulose and 0.5% citric acid.

KEYWORDS: Chlorhexidine, Cosmetic stability, Preliminar stability study, Soaps.

INTRODUCTION

The hand washing using soap degerming is essential to reduce the risk of infections and thus, the ideal is the use of antiseptic liquid soaps. It is usual to use antiseptic liquid soaps prior to surgery. Among the formulations used are soaps containing 2% chlorhexidine gluconate.[1,2]

Liquid soaps are products that are gaining wide appreciation by the consumer due the best fixing of perfume and attributes such as hydration and smoothness to the skin. These products show very similar composition of shampoos, with only minor differences, for example, the amount of foam and smoothness. These characteristics are highly valued because it makes the active content, and conditioning agents are added in higher concentration. Liquid soaps can be directed to body, facial hygiene (especially for oily or young skin) and hand hygiene,[3,4]

The formulation of liquid soap is generally constituted by a surfactant, for example, lauryl ether sodium sulfate and cocamide propyl betaine as surfactants, which are used in order to ensure the stability of the foam and increase the viscosity of liquid soap. Also part of the composition of these products thickeners raw materials, preservatives, sequestering agents, active ingredients and fragrance.[5]

The surfactants are substances that modify the surface and interfacial tension of molecules can be classified into anionic, cationic, nonionic and amphoteric surfactants according to their behavior in aqueous solution. They are responsible for one of the most important feature and in a desired a liquid soap, the removability of the dirt by forming micelles.[6,7]

The thickeners assist in thickening, since the consumer correlates this property to the quality of the product. The addition of sodium chloride (NaCl) is one of the most common methods to increase the viscosity of liquid soap formulations. But due to the fact that chlorhexidine is incompatible with anions, it is not inadvisable to include NaCl in this type of formulation. Thus, another way must be found to thicken liquid soap, an alternative is hydroxyethylcellulose (HEC) having no ionic character and is compatible with the formulation.[8]

Chlorhexidine, being a base that has cationic character, does not bring satisfactory results when used in conjunction with anionic surfactants. Surfactants suitable for chlorhexidine formulations are nonionic and amphoteric surfactants such as the diethanolamide of coconut fatty acid and cocamide propyl betaine.[9]

The chlorhexidine digluconate solution at low concentrations acts as bacteriostatic agent, and at higher concentrations acts as a bactericidal agent. Also, chlorhexidine may also inhibit bacterial adhesion to surfaces through competition with calcium.[10]

Generally, chlorhexidine gluconate solution concentration ranges from 0.02 to 5% and may be employed for various purposes. The use of chlorhexidine is very broad and can be employed for cleaning surfaces, clothing and equipment in hospitals. It is also used for antisepsis of the skin, mucous membranes and hands and for the treatment of wounds.[11,12,13]

The use of chlorhexidine for handwashing is safe and skin absorption is very small. However, it can cause skin irritation, and this irritation is concentration-dependent, most likely for products containing 4% chlorhexidine and when used often.[14]

The addition of active in cosmetics tends to cause instability problems due to physico-chemical incompatibility, or even oxidation that occurs in the storage period. These are factors that limit the incorporation of assets in cosmetic formulations.[15]

The development of an appropriate formula of liquid soap as a vehicle for chlorhexidine requires in-depth study on compatible components for the asset is preserved, it is also necessary to carry out stability tests.[16]

To perform the screening of cosmetic formulations, it is proposed that a few preliminary tests stability immediately after production. Samples of the formulations must be subjected to centrifugation test and the test of thermal stress, these tests will evaluate if the samples had some instability, or phase separation. If it remains homogeneous, it is approved for stability testing. If you have any changes, this formulation should be reworded.[14]

The preliminary stability test can be considered of auxiliary character in product development. The test consists of subjecting the sample to extreme temperature conditions, in order to speed up possible cases of instability, with the purpose of assisting in the screening of formulations.[17]

In view of this, this study aimed to develop eve twelve liquid soap formulations containing 2% chlorhexidine gluconate. After the preparation of formulations with different concentrations of hydroxyethylcellulose and citric acid, the samples were subjected to centrifugation test and thermal stress test.

MATERIALS AND METHODS

- ***Preparation of formulations***

Aliquots of 200 ml of twelve different test formulations were prepared with varied concentrations of hydroxyethylcellulose (HEC) and citric acid. The concentrations of all formulations can be observed in Table 01.

Table 01. Qualitative and quantitative description of the components of the proposed formulations.

Components	Formulations (%)											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Diethanolamide of fatty coconut acids	5	5	5	5	5	5	5	5	5	5	5	5
Cocoamide propyl betaine	5	5	5	5	5	5	5	5	5	5	5	5
Hydroxyethylcellulose (HEC)	1	1	1	1	1,3	1,3	1,3	1,3	1,5	1,5	1,5	1,5
Citric acid 20% solution	0,3	0,5	0,7	0,9	0,3	0,5	0,7	0,9	0,3	0,5	0,7	0,9
Glycerin	5	5	5	5	5	5	5	5	5	5	5	5
Methylparaben	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2	0,2
20% Chlorhexidine solution	10	10	10	10	10	10	10	10	10	10	10	10
Purified water	73,5	73,3	73,1	72,9	73,2	73	72,8	72,6	73	72,8	72,6	72,4

- ***Centrifugation Test (CT)***

Were weighed about 10 g of each of the test formulations to carry out the centrifugation test under the following conditions: 3,000 rpm for 30 minutes at ambient temperature.[18] The tests were carried out immediately after preparation of the formulations.

After the test, samples of formulations were analyzed for appearance and classified as heavily modified (IM), modified (M), slightly modified (LM) and normal, without changes in appearance (N).[18]

- ***Thermal Stress Test (TST)***

Were weighed approximately 10 g of the formulations in test tubes. Samples of the formulations were subjected to thermal stress in thermostated bath at controlled temperature range 40-80 °C, progression 10 ºC every 30 minutes. Samples were analyzed at the end of 80 °C. The tests were carried out immediately after preparation of the formulations.[19] After the test, the samples were evaluated as modified (M) to normal (N), no changes in appearance of the samples.

RESULTS AND DISCUSSION

The centrifugation and heat stress are tests carried out in extreme conditions that can provide the product instability indications, showing whether or not changes in the composition of the formulations.[17]

- ***Centrifugation Test (CT)***

The samples were evaluated according macroscopic parameters as evaluation of the appearance. The results obtained in the centrifuge test are presented in Table 02.

Table 02: Results of analysis of samples subjected to centrifugation test.

Formulations											
F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
IM	N	IM	IM	IM	IM	IM	IM	IM	IM	IM	IM

Of all the twelve samples tested, eleven samples (91.6% of samples) showed strongly modified, occurring phase separation, as can be seen in Figure 01. Only the F2 formulation showed no phase separation (Figure 01), behaving optimally for this test, showing good appearance and homogeneous incorporation of the active ingredients, suggesting an adequate stability.

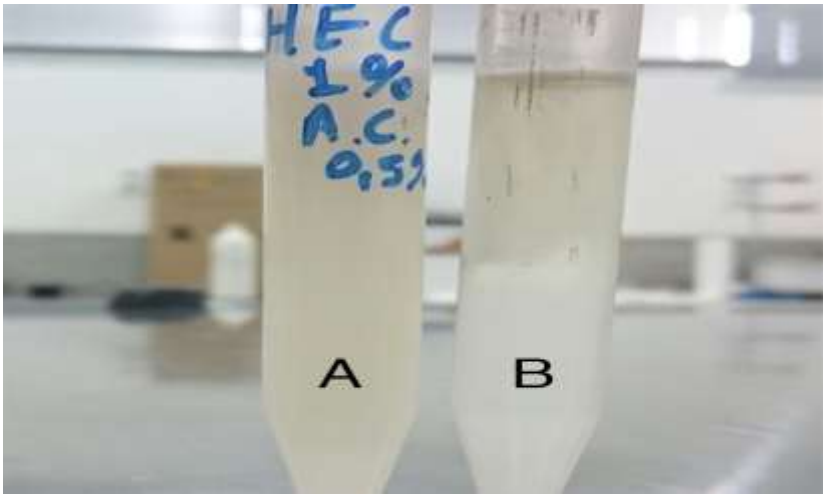

Figure 01. Samples after centrifugation test. A: Sample considered appropriate (F2). B: Sample considered inappropriate, phase separation occurring. All formulations except the formulation F2, showed a pattern equal to tube B.

The non-occurrence of phase separation does not ensure its stability only indicates that the product can be subjected, without reformulation, to stability tests.[17]

- ***Thermal Stress Test (TST)***

The results of samples analysis of the formulations which were submitted to heat stress test can be observed in Table 03.

Table 03: Results of the analysis of samples submitted to thermal stress test.

Formulações-teste											
F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**	**F10**	**F11**	**F12**
M	N	M	M	M	M	M	M	M	M	M	M

Among the samples submitted to thermal stress test, only the F2 formulation showed no phase separation, as can be seen in Figure 02. All other samples showed phase separation (Figure 02).

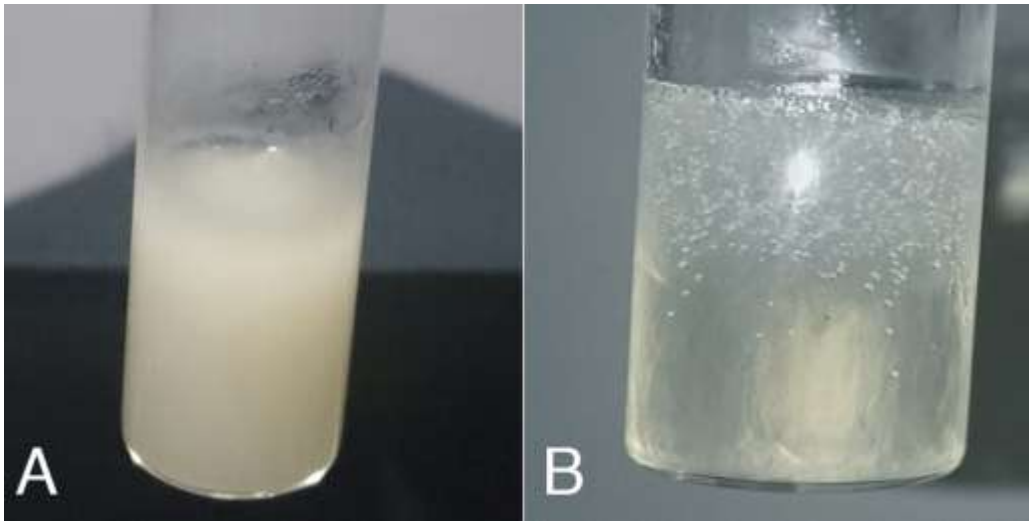

Figure 02. Samples after the thermal stress test. A: Sample considered appropriate (F2). B: Sample considered inappropriate, with separation of phases. All formulations except the formulation F2, showed a pattern equal to tube B.

The thermal stress accelerates the process of degradation of formulation components. The non-occurrence of phase separation should be indicative of the stability of the test product.[17]

Preliminary stability tests performed as the centrifugation test and the thermal stress test made it possible to identify signs of instability in most samples submitted for testing. Signs of instability were identified as phase separation and formation of lumps. Only one of the test formulations was considered approved, showing no signs of instability.

According to the Cosmetic Stability Guide (2004), preliminary studies are the first testing sequence suggested for evaluate the stability of cosmetic products. Preliminary testing is also known as a screening test, provide information about the stability of the product in the shortest time possible. For this, samples must be stored in conditions that accelerate the possible changes that may occur in the formulation.[18]

For ensuring those proper characteristics of conservation and storage, it is necessary to pay attention to the fact that chlorhexidine can interact with the glass, promoting its precipitation. For this reason must be stored in plastic bottles PVC or PET type, amber, to remain protected from light as it undergoes photodegradation, besides the recommendation for the product storage at ambient temperature.[20,21]

CONCLUSION

The preliminary stability study performed in formulations with different percentages hydroxyethylcellulose and citric acid enabled the selection of the best formulation for the development of liquid soap containing 2% chlorhexidine digluconate.

The results were adequate and satisfactory in the stability study for the formulation F2, which showed no signs of instability after the centrifugation test and thermal stress test. The eleven other formulations showed phase separation.

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