Systematic development of emulsion for treatment of diaper dermatitis

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INTRODUCTION

Diaper dermatitis, popularly known as diaper rash[1-2], is a frequent pathology, especially in pediatric clinics and dermatology. It is a major cause of complaints from mothers[2-7]. This skin disease is mainly present on the first two years of life[1-4, 8-10], without predilection for race, gender or social standard.

To avoid diaper dermatitis, it is recommended, at each diaper change, the use of a water-repellent emollient (protective ointment) onto the infant's skin. This is the reason for the increase of the use of commercially available ointments. These are most often formulated with large quantities of powder (20 - 50%) and zinc oxide in an oily vehicle[2, 4].

Zinc oxide provides a water-impermeable barrier that reduces friction and maceration, protecting the skin, and acting as a physical barrier against irritants. It is effective for prophylaxis or treatment of moderate diaper dermatitis, but when the skin is severely affected by the presence of a fungal agent, such as *C. albicans,* which is present in 41% to 77% of children with this condition, an antifungal agent is necessary. In such a case it is recommended the use of nystatin, which has been used for nearly 50 years for the treatment of *Candida* infections and revealed to be safe and effective in the treatment of cutaneous candidiasis in children[2, 11].

Currently there are several products for the prevention and/or the treatment of diaper dermatitis. The composition of these products varies according to the manufacturer and most of them are running in ointments. Some zinc oxide products were combined with nystatin (eg Dermodex® - Prevent), or vitamins (eg Hipoglós® - Procter & Gamble), or a combination of these two components (eg Johnson's® Baby - Johnson & Johnson). Modern formulations that have protective properties, such as antifungal and anti-inflammatory ones, would be of great value to the treatment[2].

A new issue on the development of diaper dermatitis' products is the use of sesame (*Sesamum indicum* L., Pedaliaceae) oil. The oil derived from its seeds, rich in poly-unsaturated fatty acids, is increasingly used in industries of food, cosmetics and pharmaceuticals[12].

Therefore, the aim of this work was the development of emulsions containing zinc oxide and sesame oil as internal phase for future use in diaper dermatitis. The idea is to improve the therapeutic use of the sesame oil. Also, a series of assay was carried out to efficiently evaluate the stability of the emulsions.

MATERIAL AND METHODS

Fourteen emulsions were made with sesame oil (VitalAtman - Brasil) as oily phase, Tween® 20 and Span® 80 as surfactant system, and purified water as the aqueous phase. A group of seven emulsions were produced varying the HLB (hydrophilic-lipophilic balance) value, the concentration of surfactants and the presence or absence of zinc oxide (table 1). These emulsions were made by the phase inversion method. The aqueous and oily phases were separately heated at 70 ± 2° C and then the aqueous phase was slowly added to the oil phase under constant stirring (13000 rpm) for ten minutes. Following, zinc oxide at a concentration of 10% was added into a half volume of each formulation and the preparations were submitted to other ten minutes of mechanical stirring using a homogenization apparatus, obtaining thus a total of fourteen formulations.

1 - Intrinsic stability: For each emulsion, sample vials were filled with 15ml of the emulsion and then hermetically closed. They were stored vertically at room temperature (25 °C) and were observed at time +1; +2; +4; +6, and +24 h. Changes as phase separation or creaming rate were recorded.

2 - Stability under storage: Twelve sample vials were filled as described in Section 1. Three were stored vertically at room temperature (25 °C), three in a hot air oven at 45 ºC ± 2 and three at 4 ºC ± 2. Observations were made each week for 8 weeks.

3 - Stability under centrifugation: Four centrifugation vials were filled with 5ml of emulsion and underwent a centrifugal acceleration of 3,500 rpm for 30min (BioEng, Model BE 5100). To avoid modifications induced by possible heating, the temperature was measured in one tube at the end of the experiment. It should not exceed 30 ºC.

4 - pH: The P 2000 Gehaka pHmeter was used for the determination of the pH value of the emulsions at room temperature (25 ºC).

5 - Conductivity: The DM 32 Digimed conductivimeter was used for the determination of the conductivity value of the emulsions at room temperature (25 ºC).

6 - Freeze/thaw cycles: Three samples vials filled with the emulsion and hermetically closed were vertically stored for 16 h in a freezer at −15 ºC and then for 8 h at room temperature (25 ºC). The emulsion was observed and any change was recorded. This cycle was repeated four times.

RESULTS AND DISCUSSION

All emulsions were prepared in triplicate and analyzed by centrifugation and visual characterization 24h following their production. After microscopic analysis for monitoring the intrisic stability and stability under storage, all emulsions exhibit normal aspect and white color.

Resistence of an emulsion to centrifugation depends not only on the difference of density between the oily and aqueous phases, but also on the resistance on the interfacial film. Therefore, for similar formulations that exhibit small density differences, the stability under centrifugation reflects the strength of the interfacial film. The stability study under centrifugation at 3,500 rpm gives excellent information about the stability of the formulations compared to the creaming volume percentages. After centrifugation all formulations show a light tendency to creaming, except F1, F8 and F10.

Several emulsions that underwent freeze/thaw cycles presented damage, which was dependent on the formulation characteristics. On formulation F14 rupture occurred after one cycle; formulations F6 and F7 creamed after two cycles. All other formulations remained stable during the study (five cycles).

Measurements of pH and conductivity are useful data especially for quality assurance. Their variations may explain some expected differences observed between formulations. The pH values of the formulations remained in the range of 4,3 - 5,5 for blanch emulsions, and 7,4- 7,6 for zinc oxide loaded ones. The electric conductivity values remained in the range of 35,6 – 49,1 µS/cm for blanch emulsions, and 42,57 e 84,72 µS/cm for the loaded ones, which are quite compatible to the skin. The monitoring of stability through the values of pH and electrical conductivity revealed that the formulations remained stable during the study period.

CONCLUSION

The results reveal that all the formulations containing zinc oxide presented a good stability. Probably the powder content on these formulations was the reason for such improvement on the stability. Additionally, the presence of zinc oxide was responsible for the increase on the pH and conductivity of the formulations. These results also confirmed the potential of the sesame oil as a formulation component for therapeutic emulsions and its viability on zinc oxide containing formulations. In fact, zinc oxide on sesame containing emulsions improves its stability.

FIGURES AND TABLES

Table 1. Composition of emulsions formulations.

Formulation	Formulation composition (%)					
	HLB	Oil	Span 80	Tween 20	Water	Zinc Oxide
F1	16.70	54.00	-	14.00	32.00	-
F2	15.46	43.00	1.70	15.30	40.00	-
F3	14.22	59.00	2.60	10.40	28.00	-
F4	12.98	54.00	3.00	7.00	36.00	-
F5	11.74	53.00	4.00	6.00	37.00	-
F6	10.50	54.00	5.00	5.00	36.00	-
F7	9.26	57.00	3.60	2.40	37.00	-
F8	16.70	48.60	-	12.60	28.80	10.00
F9	15.46	38.70	1.53	13.77	36.00	10.00
F10	14.22	53.10	2.34	9.36	25.20	10.00
F11	12.98	48.60	2.70	6.30	32.40	10.00
F12	11.74	47.70	3.60	5.40	33.30	10.00
F13	10.50	48.60	4.50	4.50	32.40	10.00
F14	9.26	51.30	3.24	2.16	33.30	10.00

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