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Multi-Response Optimization in the Formulation of a Topical Cream from Natural Ingredients

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Received: 1 November 2017; Accepted: 29 December 2017; Published: 5 January 2018

Abstract: The aim of this research was to study the effect of local raw materials on the formulation of a base cream formulation and determine the optimum proportion of each material that gives the required properties. Physicochemical properties of cream formulations can be affected by their viscosity, spreadability, and particle size. The quality of the base cream is directly linked to the basic material used in the formulation. Screening of independent factors, namely oil phase (sesame oil, soybean oil, and liquid paraffin), aqueous phase (*Aloe vera* gel, propylene glycol, and glycerol), and surfactant (soy lecithin, tween, and soy lecithin/tween) was done to choose the best raw material required for the preparation of the base cream. Based on the screening criteria, sesame oil, *Aloe vera* gel, and soy lecithin were chosen as the best local raw materials. Using a multi-response optimization, the mixing fractions of sesame oil, *Aloe vera* gel, and soy lecithin were found to be 24%, 28%, and 10%, respectively. This base cream can be used as a suitable matrix for formulation in the cosmetic and pharmaceutical industries.

Keywords: local raw materials; formulation; base cream; multi-response optimization

1. Introduction

Topical products are liquid or semisolid preparations, such as ointments, lotions, gels, and creams [1]. Creams are usually emulsions, which are thermodynamically unstable and consist either of two-phase systems (oil in water or water in oil), in which one is dispersed in the form of small droplets throughout the other [2]. To produce commercial products with sufficiently long shelf lives to environmental stresses, it is necessary to incorporate stabilizers, such as thickening agents, gelling agents, weighting agents, ripening inhibitors, and emulsifiers [3]. The emulsifying agent possesses hydrophilic and hydrophobic groups [4], adsorbed at the interface of water and oil, and reduces the interfacial tension. Emulsifiers are particularly important ingredients for forming stable emulsions with appropriate shelf lives and functional attributes. Most industrial emulsifiers, currently used to stabilize oil-in-water emulsions, are synthetic surfactants (such as Tweens and Spans [5]) or animal-based emulsifiers (such as gelatin, egg protein, whey protein, and caseinate [6]). However, there is an increasing consumer demand for more natural, environmentally friendly, and sustainable commercial products [7]. Many manufacturers are reformulating their products to replace the synthetic surfactants with more label-friendly natural alternatives [8] or to replace animal proteins from with plant proteins [9,10]. Generally, manufacturers would often like to create new products entirely from natural ingredients so that they can make "all-natural" claims on their labels. On the other hand, the

physical stability of emulsions is an important factor when pharmaceutical formulations are considered as drug delivery concepts.

In recent years, the interest in the use of natural polymers in pharmaceutical, nutraceutical, and cosmetic formulations has markedly increased [11]. Lowering interfacial tension eases droplet break-up, and interfacial viscosity provides stability. Silva et al. and Alvarez Lorenzo et al. have reported the use of protein-based emulsion hydrogels [12,13], while Tang et al. have used soy protein isolate for stabilizing emulsion hydrogels [14].

Lecithin is a naturally occurring zwitterionic phospholipid-based liquid surfactant (extracted from egg and soybean). It has been extensively studied as a structuring agent for food, pharmaceutical, and cosmetic applications [15]. Lecithin derived from soybean has been reported to be biocompatible and has been used for transdermal drug delivery applications. Lecithin based on organogels has been reported by many researchers [16], but emulsion hydrogels have not been explored much yet.

Aloe vera Burm (liliaceae family) is an imperative functional ingredient exhibiting remarkable biological efficacy to the cosmetic, pharmaceutical, and food industries. For centuries, this plant has been used for its medicinal and therapeutic functions without scientific analysis for its health, beauty, and skin care properties. The leaf consists of pericyclic cells and the inner central area of the leaf (i.e., the gel) along with the leaf extract, juice, and polysaccharides. *Aloe vera* gel is used as a base in many cosmetic formulations.

Emulsions are widely used for the treatment of dry skin and emollient applications. A cosmetic formulation including the active principle of strictly natural origin is designed to protect the skin against exogenous or endogenous harmful agents. Due to the importance of soy lecithin and the skin care benefits of *Aloe vera*, the purpose of this study was to develop a stable cream emulsion with local raw materials. The effects of different factors of each phase on the stability and viscosity of the emulsion were analyzed. A multi-response optimization was done to obtain a combined optimum proportion of local materials in each phase. In this methodology, the study of an ingredient's effect on viscosity, particle size, and spreadability is an attempt to find the formulation that produces the best response.

2. Materials and Methods

2.1. Materials

Sesame and soybean oil were extracted by the soxhlet method. Lecithin was obtained by ethanolic extraction from soy residue after the defatting of soy powder with hexane. Matured *Aloe vera* leaves were purchased from the local market of Bini-dang, Ngaoundere, Cameroon. All of the other reagents, such as liquid paraffin, glycerol, Tween 80, and propylene glycol, were purchased from VWR International Co (VWR).

2.2. Methods

2.2.1. Preparation of local materials for formulation

Extraction of sesame and soybeans oil: Sesame and soybean seeds were purchased from a local *market of Bini-dang, Ngaoundere*. The seeds were sorted to eliminate damaged grains and dirt. Seeds in good condition were washed thoroughly with clean water and sun dried in the open. All apparatus were washed and oven dried, and the soxhlet apparatus was set up in readiness for the experiment. The seeds were grounded mechanically, while soybean seeds were de-husked before grinding. Five hundred grams of each powdered sample was placed in a thimble made from thick filter paper and inserted into the center of the extractor. The soxhlet (1 L capacity) equipped with a condenser was placed onto a flask containing the hexane. The soxhlet was heated to 65 °C and allowed to reflux for about 8 h. It was then removed from the tube, dried in the oven, cooled in the desiccators, and weighed again to determine the amount of oil extracted [17].

For lecithin: Lecithin was obtained by ethanolic extraction from soy residue after the defatting of soy powder with hexane. The soxhlet was heated to 80 °C and allowed to reflux for about 24 h.

Obtention of *Aloe vera* gel protocol described by [18]: Leaves of *Aloe vera* were cut, washed, and then sliced an inch on both the upper and lower sides. The leaves were further cut and the pulp was removed thereafter. The pulp obtained was further crushed in a mechanical crusher. After the crushing of the pulp it was filtered in order to remove the attached fibres. The obtained sap was stored for future use.

Additional information: The viscosity of the sesame oil was 54.2 cP. The viscosity of the soybean oil was 39.5 cP. The moisture content of the *Aloe vera* gel was 92.23%.

2.2.2. Screening of Factors of Each Phase

The different variables used in this study are shown in Table 1.

Table 1. Different variables.

Phase (Percentage)	Material	Coded Variable	Level of Variable
Oil phase (20%)	Soybean oil	X_1	1
	Sesame oil		2
	Liquid paraffin		3
Aqueous phase (30%)	*Aloe vera* gel	X_2	1
	Glycerol		2
	Propylene glycol		3
Emulsyfing phase (8%)	Lecithin	X_3	1
	Tween		2
	Lecithin/tween		3

In fact, the amounts of the three components of the emulsion (oil phase (X_1), aqueous phase (X_2), and emulsifying phase (X_3) (Table 1)) were selected as the factors to systematically optimize the dependent variables (creaming index, viscosity, and spreadability). All other formulation and processing variables (Water 31.7%, Acidifiant 0.3%, Beeswax 10%) were kept invariant throughout the study. The levels of the three factors were selected on the basis of the preliminary studies carried out before implementing the experimental design. The screening plan proposed by the STATGRAPHICS Centurion program gave 27 experiments.

2.2.3. Experiment for the Optimization of the Base Cream Formulation

Screening was done to permit us to choose the best mixture with the selected local raw materials of the oil, aqueous, and emulsifying phases. With them, the following domain with constraints (Table 2) was used. It was defined according to previous experiments and the literature review.

Table 2. Implicit Domain for optimization plan.

Raw Material	Abbreviation	Lower Limit (%)	Upper Limit (%)
Selected oil phase	X_1	20	25
Selected aqueous phase	X_2	28	32
Selected emulsifying phase	X_3	8	10

Based on the above implicit plan proposed by the STATGRAPHICS Centurion program, fifteen experiments were obtained for optimization. The responses were spreadability, viscosity, and particle size.

2.2.4. Preparation of Emulsion Base

The emulsion preparation consisted in the simultaneous mixture of phases. Eight grams of emulsifier and 10 g of beeswax were dissolved in 20 g of oil phase (Part A) and heated to 75 °C. Water (31.7 g) and citric acid (0.3 g) were dissolved in 28 g of the aqueous phase (Part B) and heated to 75 °C. After heating, the aqueous phase was gradually added to the oil phases and stirred with a high shear mixer for 5 min. Once the emulsion presented a uniform appearance, it was mixed manually [19].

2.2.5. Response Parameters

The response parameters studied included an analysis of the creaming index, viscosity, spreadability, and particle size.

All analyses were done 24 h after the preparation of different emulsions at room temperature.

Creaming Index

Direct optical observations were employed to determine the instantaneous heights of the emulsion and the aqueous phase inside the glass vessel. This was done with the help of a graduated scale. The creaming index (CI) was estimated using the formula: $\%CI = \left(\frac{CC}{CT}\right) * 100$, where CC is the total height of the cream layer, and CT is the total height of the emulsion layer [20].

Viscosity

Viscosity was determined with the help of a CAP-2000 Brookfield viscometer using the method [21]. Test samples were taken in clean and dry 250 mL beakers, and the viscosity of a test sample was determined by the standard operating procedure for the Viscometer using spindle N° 4. This spindle was used to determine the viscosity of the sample at 60 rpm. The reading at 100% torque was noted. Samples were measured at 25 ± 1 °C. The values were read in centipoise.

Spreadability

The spreadability of the formulation was determined by an apparatus which was set up in the laboratory. The cream emulsion was placed between two glass slides, a 1000 g mass was placed on the slides for 5 min to compress the sample to a uniform thickness, and excess cream was scraped off. A 120 g mass, M, was tied to the upper slide. The time in seconds required to move the slides across a distance of 10 cm was taken as the measure of spreadability [22]. The following formula was used for the calculation of Spreadability:

$$S = \frac{M \times L}{T}$$

where S is Spreadability, M is the mass tied to the upper slide in g (120 g), L is the length of the slide in 10 cm = 10×10^{-2} m, and T the time taken to separate two slides. Spreadability was recorded in g·m/s.

Particle Size Determination

The particle size of the emulsions was determined using a Malvern particle size analyser (Mastersizer 2000S, Malvern Instrument Ltd., Malvern, UK). Emulsions were added, in a dropwise manner, to deionized water in the dispersion cell of the instrument. The optical parameters selected were as follows: a relative refractive index of 1.449, a particle absorbance of 0, and a continuous phase refractive index of 1.33. Each sample was analyzed three times and the data are presented as the average. The average droplet size was characterized by mean diameters related to the volume. All measurements were carried out at 25 °C. The results of the particle size are expressed as Z-average size [23].

2.2.6. Microstructure Observation

The morphology of some selected emulsions was observed using an optical microscope (Axiophot, Germany) at a 40× magnification. Prior to the microscopic observation, the emulsion samples were shaken gently. Subsequently, a drop of the emulsion was placed onto a microscope slide and covered with a cover slip. Photomicrography images of the emulsion were captured using digital image processing software.

2.2.7. Statistical Analysis

Four experiments were carried out at each experimental design point and the mean values are stated as observed responses. Experimental runs were randomized to minimize the effects of unexpected variability in the observed responses. Comparison of means was performed by one-way analysis of variance (ANOVA) followed by Duncan's test. Statistical analyses ($p < 0.05$) were performed using Statgraphics centurion software (Version XVI.I, Statgraphics Technologies Inc. The Plains, VA, USA).

3. Results and Discussion

3.1. Screening of Base Cream Materials

The results of the analysis of different formulation bases aimed at choosing the best oil, aqueous, and emulsifying phases are shown in Table 3. The properties considered during the analysis were the creaming index, the spreadability, and the viscosity. The experimental results obtained were between 0 and 28.33%, 9.0 and 31.02 g·cm/s, and 290 and 480 cP (centipoise) for the creaming index, the spreadability, and the viscosity, respectively. It is important to analyze each response individually to obtain good properties for the emulsion base.

Table 3. Screening design for different ingredient phases of the base cream formulation.

Runs	Oil Phase	Emulsifying	Aqueous Phase	Creaming Index (%)	Spreadability (g·cm/s)	Viscosity (cP)
1	1	3	1	0.0 ± 0.0	31.02 ± 1.12	360 ± 10
2	2	3	1	0.0 ± 0.0	20.99 ± 1.01	340 ± 7
3	1	1	1	8.33 ± 0.12	20.46 ± 1.09	320 ± 5
4	1	2	1	0.0 ± 0.0	22.39 ± 1.15	328 ± 8
5	2	1	1	16.66 ± 0.14	17.87 ± 1.15	415 ± 12
6	2	2	1	28.33 ± 0.10	15.07 ± 0.51	425 ± 11
7	3	1	1	25.00 ± 0.11	22.60 ± 1.14	229 ± 8
8	3	2	1	16.67 ± 0.14	21.57 ± 1.17	275 ± 6
9	3	3	1	10.00 ± 0.05	21.99 ± 0.25	290 ± 4
10	1	1	2	20.00 ± 0.13	9.043 ± 0.05	370 ± 6
11	1	2	2	1.66 ± 0.05	20.62 ± 1.01	367 ± 5
12	1	3	2	1.66 ± 0.06	22.18 ± 1.10	315 ± 11
13	2	1	2	15.67 ± 0.17	12.31 ± 0.053	480 ± 14
14	2	2	2	8.33 ± 0.02	14.90 ± 0.95	410 ± 11
15	2	3	2	1.66 ± 0.05	19.27 ± 1.10	419 ± 9
16	3	1	2	20.00 ± 0.17	20.44 ± 1.10	420 ± 7
17	3	2	2	1.66 ± 0.03	22.60 ± 1.11	412 ± 10
18	3	3	2	0.0 ± 0.0	19.64 ± 1.12	390 ± 9
19	1	1	3	8.33 ± 0.11	18.37 ± 1.10	415 ± 11
20	1	2	3	0.83 ± 0.01	18.96 ± 1.09	419 ± 12
21	1	3	3	0.0 ± 0.10	15.70 ± 0.05	417 ± 10
22	2	1	3	15.00 ± 0.11	13.75 ± 0.05	412 ± 8
23	2	2	3	15.00 ± 0.10	21.00 ± 1.03	421 ± 10
24	2	3	3	3.33 ± 0.09	22.19 ± 1.07	450 ± 14
25	3	1	3	13.33 ± 0.14	22.39 ± 1.12	409 ± 6
26	3	2	3	1.60 ± 0.02	19.64 ± 1.08	419 ± 8
27	3	3	3	8.33 ± 0.09	17.70 ± 1.05	290 ± 2

3.1.1. Effect of Different Phases on Creaming Index

The creaming index was found to be in the range of 0 to 28.33% depending on the material used at each phase (Table 3). The Pareto chart indicates that each material phase possesses a significant influence on the creaming index. The influence of the different factors on the creaming index are shown in Figure 1.

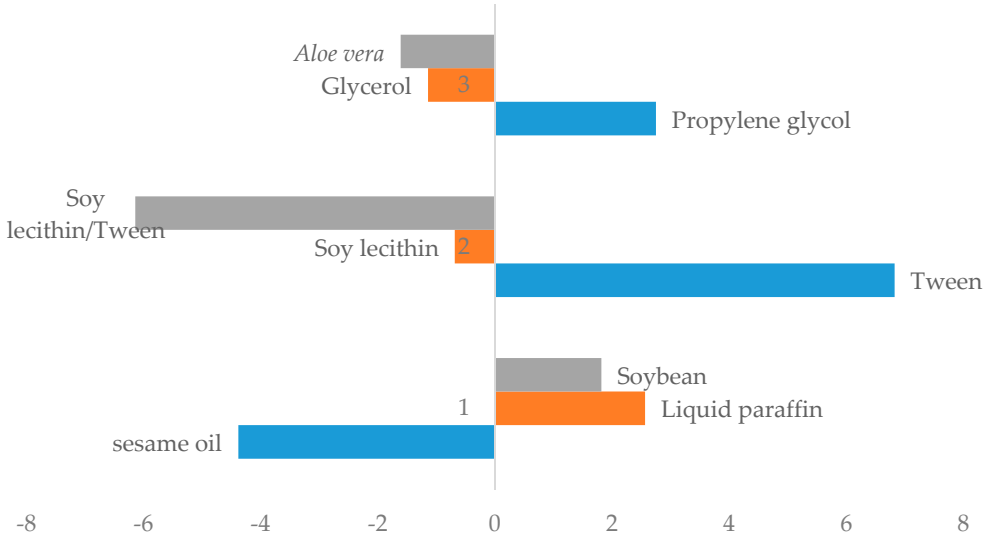

Figure 1. Effect of ingredient phases on the creaming index.

In this figure, it can be observed that the effects of the sesame oil, soy lecithin, glycerol, *Aloe vera* gel, and soy lecithin/tween combination contribute to reducing the creaming index to a much lower value than those of the soybean oil, tween, liquid paraffin, and propylene glycol. Therefore, sesame oil, *Aloe vera* gel, and the combination of soy lecithin/tween considerably decrease the creaming index, that is, the degree of destabilization of the emulsion. This can be due to the fact that soy lecithin has two tails, which are C16–C18 in length, and one of the tails has two cis unsaturations [24], which stabilizes better the emulsion oil in water [25]. In fact, soy lecithin has a low tendency to desorb, which fortifies the interfacial film, and the large headgroup of Tween provides steric repulsions between the oil droplets and prevents their coalescence [26]. On the other hand, soy lecithin alone decreases the creaming index, but the combination of lecithin and tween decreases the creaming index more. Soy lecithin and tween blends show a synergistic effect, i.e., their combination is an effective emulsifier, but neither soy lecithin or tween is effective on its own. So, it will be necessary to combine both of them for good cream stability.

3.1.2. Effect of Different Phases on Spreadability

Spreadability is the ability of a cream to spread on the skin. It plays an important role in the administration of a standard dose of a medicated formulation to the skin and the efficacy of a topical therapy. If spreadability decreases, the topical cream is good because applying it to the skin is easy [27]. The spreadability values were found to be in the range of 9.0 to 31.02 g·cm/s, depending on the material of each phase (Table 3). The influence of the different factors on spreadability is shown in Figure 2.

It can be observed that synergism could be obtained by using a combination of sesame oil, soy lecithin, and *Aloe vera* gel. This effect can be explained by the fatty acid present in the sesame oil and soy lecithin. In fact, sesame oil has 96% of total fatty acids [27] and lecithin has 5.68% free fatty acids. The spreadability of creams decreases with increasing content of unsaturated fatty acids [28].

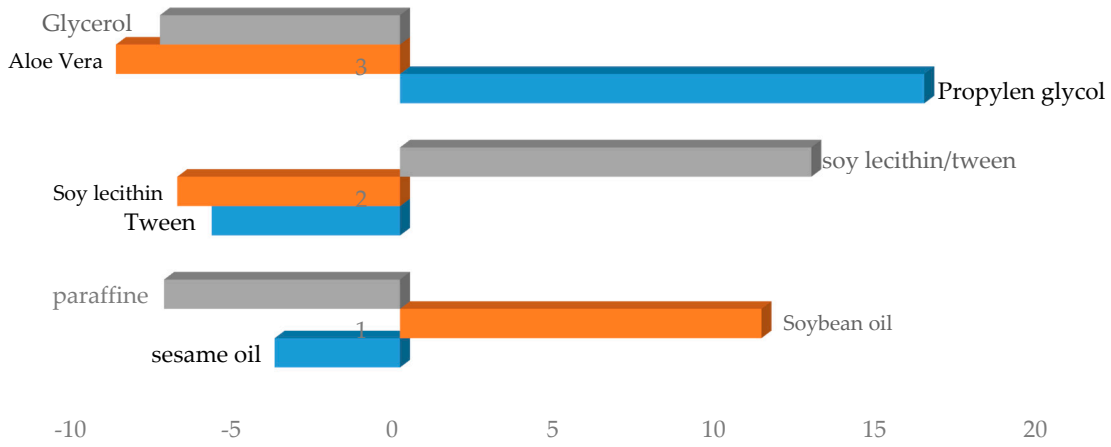

Figure 2. Effect of ingredient phases on spreadability.

3.1.3. Effect of Different Phases on Viscosity

Viscosity was found to range from 290 to 480 cP depending on the material of each phase (Table 3). The Pareto chart indicates that each phase possesses a significant influence on viscosity. The influence of the different factors on viscosity is shown in Figure 3.

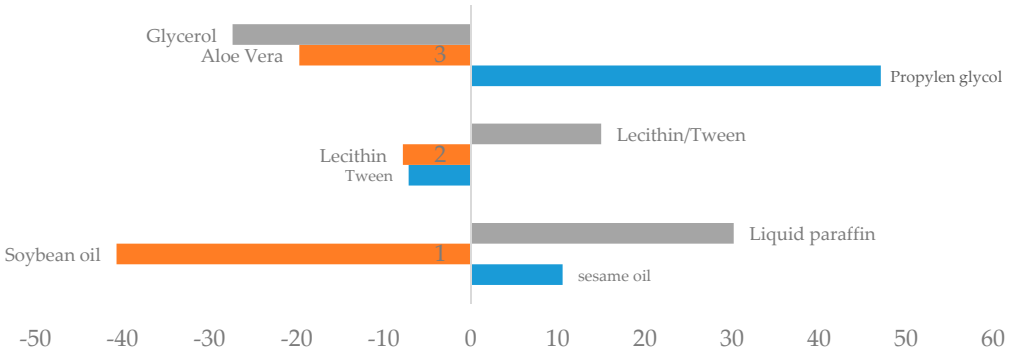

Figure 3. Effect of ingredient phases on viscosity.

Viscosity is a measure of the resistance of a fluid to flow. The more viscous a liquid, the greater is the quantity of energy required to produce a desired state of flow. Thereby, liquid paraffin and propylene glycol have viscosities that are not interesting for our desired product.

On the other hand, soy lecithin localizes on the surface of the emulsion particles, reduces interfacial free energy, provides a mechanical barrier to coalescence [29], and reduces viscosity. However, the addition of tween results in a better end product, perhaps due to synergistic effects [30]. The cream retained the desirable effects of lecithin but the lecithin did not alter the type of emulsion in any significant or detrimental way.

Viscosity decreases with *Aloe vera* gel. This is mainly due to the presence of polysaccharides composed of a mixture of acetylated glucommannans that lose their properties after extraction, apparently due to enzymatic degradation [31]. It is important to associate it with another gel to maintain its viscosity.

The screening of factors allowed us to choose sesame oil for the oily phase, *Aloe vera* gel for the aqueous phase, and the combination of soy lecithin/tween for the emulsifier. We will add natural gum from local plants to stabilize the *Aloe vera* gel.

3.2. Correlation between Responses

Correlation studies of different responses are given in Table 4.

Table 4. Correlation of different responses.

Responses		Coefficient Correlation	Goal
Height	Viscosity	0.71	Moderately strong
Spreadability	Viscosity	0.95	Strong
Spreadability	Height	0.66	Average

From the table above, a strong inverse correlation was observed between spreadability and viscosity. It is in accordance with works which showed that when the viscosity of a formulation increases, the spreadability decreases and vice versa [32].

3.3. Optimization of Base Cream Formulation

The results for the optimization of the formulation matrix are shown on the table below (Table 5), we used oil phase (X_1: sesame oil), aqueous phase (X_2: *Aloe vera* gel), and emulsifying phase (X_3: soy lecithin/tween). The responses observed in the course of these analyses are spreadability, viscosity, and particle size. The experimental results obtained are between 28.95 and 154.45 g·cm/s, 83 and 840 cP (centipoise), and 8.71 and 208.93 for spreadability, viscosity, and particle size, respectively.

The maximum value for spreadability (154.45 g·cm/s) was found for Experiment 2. The maximum value for viscosity (840 cP) was seen for Experiment 15, and the maximum value for particle size (208.93) was obtained in Experiment 13. Consequently, it was indispensable to realize an optimization in order to obtain the desired properties of the base cream.

Table 5. Experimental design.

Variables Level				Responses					
				Viscosity		Spreadability		Particle Size	
N°	X_1	X_2	X_3	Observed.	Adjusted.	Observed.	Adjusted.	Observed.	Adjusted.
1	24	28	8	734	785.4	28.9	34.5	34.6	21.8
2	20	32	8	293	276.0	154.4	140.3	22.9	25.1
3	22	28	10	640	611.6	54.5	57.7	8.7	3.7
4	20	30	10	100	382.8	34.9	24.9	34.6	25.0
5	22.75	28.75	8.5	760	747.8	46.3	34.2	104.7	106.3
6	20.75	30.75	8.5	218	221.4	57	65.7	138.0	140.7
7	21.75	28.75	9.5	220	240.2	54.5	45.6	138.0	142.0
8	20.75	29.75	9.5	83	54.1	38.9	39.9	158.4	158.7
9	22	30	8	320	332.7	46.3	48.2	60.2	64.5
10	23	28	9	386.7	406.3	35.4	36.8	69.1	77.0
11	20	31	9	240.3	264.4	45	51.9	69.1	77.4
12	21	29	10	426	473.6	40.2	49.5	79.4	98.3
13	21.5	29.5	9	284	253.1	42.3	42.62	208.9	186.3
14	20	32	8	266.7	785.4	132.3	34.5	30.2	21.8
15	24	28	8	840	276.0	35.6	140.3	11.4	25.1

Table 6 presents the significance of different effects of base cream models and the indicators for the validation of the models for the different responses, respectively. Lack of fit was also given in order to check the quality of the fitted models.

Table 6. Significance of different effects of base cream models and indicators of validations.

Parameters	Viscosity		Spreadability		Particle Size	
	Coefficient	Probability	Coefficient	Probability	Coefficient	Probability
X_1	785.4		34.5		21.8	
X_2	276.0		140.4		25.1	
X_3	13,733.3		155.1		−626.1	
$X_1 \times X_2$	−792.2	0.01	−156.9	0.007	164.5	0.01
$X_1 \times X_3$	−26,590.8	0.0009	−148.2	0.2	1201.7	0.0009
$X_2 \times X_3$	−26,487.5	0.0009	−491.1	0.002	1302.3	0.0008
$X_1 \times X_2 \times X_3$	32,404.4	0.002	576.5	0.06	2048.3	0.002
$X_1 \times X_2(X_1 - X_2)$	3013.8	0.004			−287.2	0.003
$X_1 \times X_3(X_1 - X_3)$	14,610.4	0.002			−86.3	0.002
$X_2 \times X_3(X_2 - X_3)$	16,964.6	0.001			−310.2	0.0010
R^2	98.25		95.44		96.92	
R^2 adj	95.09		92.02		91.39	
Lack of fit	0.24		0.68		0.23	

3.3.1. Influence of Formulation on Viscosity

The following equation shows the cubic model obtained after the analysis of viscosity.

$$\text{Viscosity} = 785.4X_1 + 276.0X_2 + 13{,}733.3X_3 - 792.2X_1 \times X_2 - 26{,}590.8X_1 \times X_3 - 26{,}487.5X_2 \times X_3 + 32{,}404.4X_1 \times X_2 \times X_3 + 3013.8X_1 \times X_2(X_1 - X_2) + 14{,}610.4X_1 \times X_3(X_1 - X_3) + 16{,}964.6X_2\, X_3(X_2 - X_3)$$

The coefficient of determination (R^2) obtained was 98.25% for viscosity. The p-value for lack of fit was 0.05, which suggests that the model fits the experimental data. Concerning the contribution of different factors to viscosity in Figure 4 below, it is observed that the single emulsifying X_3 (10.12) and interaction between the three mixtures $X_1 \times X_2 \times X_3$ (23.88) have a positive effect on spreadability, and interaction between $X_1 \times X_3$ (19.60%) and $X_2 \times X_3$ (19.52) show the contrary.

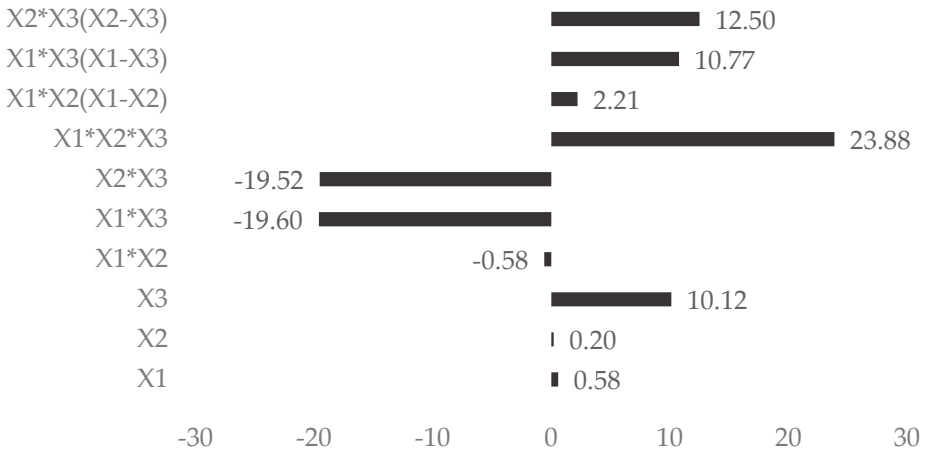

Figure 4. Contribution of factors to viscosity.

This means that the binary effects of the oil phase and emulsifying phase, the oil phase and aqueous phase, and the aqueous phase and emulsifying phase tend to reduce viscosity comparatively to each phase taken individually. This can be due to the fact that the oil phase here is sesame oil, which has in its composition a high content of fatty acids that reduce viscosity. It was observed that vegetable oils usually have higher viscosity [33], and emulsions made from them require a higher energy input

with the result in an emulsion being is that it is less stable to the migration of water in and out of the internal aqueous phase.

Concerning viscosity, the range obtained, 320 to 734 cP, is slightly comparable to the values obtained by [34], ranging from 129 to 361 cP. During their formulation, Gelucire 44/14, propylene glycol, and white petrolatum were used as the emulsifying, aqueous, and oil phase, respectively. Also, the slight difference in value can be due to the ratio (0.05:10:60) used for the formulation. From this, our formulation base cream from local raw materials could be used as a matrix in the cosmetic and pharmaceutics industries. This is because viscosity governs many properties of a formulation, such as spreadability and pourability of the product from the container [35].

3.3.2. Influence of Formulation on Spreadability

The following equation shows the special cubic model obtained after the analysis of spreadability.

$$\text{Spreadability} = 34.5X_1 + 140.3X_2 + 155.0X_3 - 156.9X_1 \times X_2 - 148.1X_1 \times X_3 - 491.0X_2 \times X_3 + 576.5X_1 \times X_2 \times X_3$$

The coefficient of determination (R^2) obtained was 92.02% for spreadability. The *p*-value for lack of fit was 0.68, which suggests that the model fits the experimental data. Concerning the contribution of different factors to spreadability in Figure 5 below, it was observed that the single aqueous phase X_2 (8.24), the emulsifying phase X_3 (9.10), and interaction between the three mixtures $X_1 \times X_2 \times X_3$ (33.84) have a positive effect on spreadability, and interaction between $X_1 \times X_2$ (9.21), $X_1 \times X_3$ (8.74%), and $X_2 \times X_3$ (28.82) show the contrary.

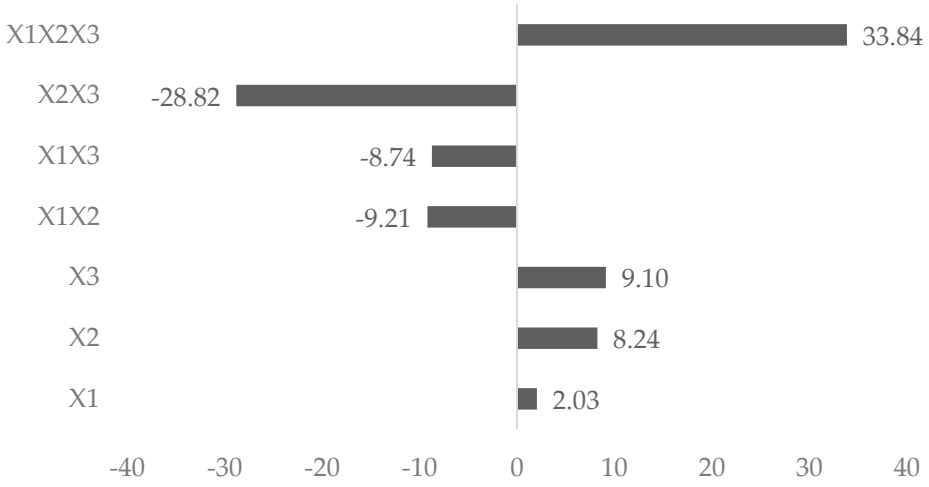

Figure 5. Contribution of factors to spreadability.

This means that the binary effects of the oil phase and aqueous phase and the oil phase and emulsifying phase exert an antagonistic effect on spreadability. The antagonistic effect can be due to the high content in unsaturated fatty acid of the oil phase (sesame oil), which tends to moderate the positive effect of the emulsifying and oil phases on spreadability. However, the strongest synergism could be obtained by the mixture of oil, aqueous, and emulsifying phases.

3.3.3. Influence of Formulation on Particle Size

The following equation shows the cubic model obtained after the analysis of particle size.

$$Y_{ps} = 21.8\,X_1 + 25.1X_2 - 626.1X_3 + 164.4X_1 \times X_2 + 1201.7X_1 \times X_3 + 1302.3X_2 \times X_3 + 2048.3X_1 \times X_2 \times X_3 - 287.2X_1 \times X_2(X_1 - X_2) - 86.2X_1 \times X_3(X_1 - X_3) - 310.2X_2 \times X_3(X_2 - X_3)$$

The coefficient of determination (R^2) obtained was 96.92% for particle size. The *p*-value for lack of fit was 0.23, which suggests that the model fits the experimental data. Concerning the contribution of different factors to particle size in Figure 6 below, it was observed that the single emulsifying X_3 (10.31) has a negative effect on particle size and interaction between $X_1 \times X_3$ (19.73%), $X_2 \times X_3$ (21.44), and interaction between the three mixtures $X_1 \times X_2 \times X_3$ (33.72) show the contrary.

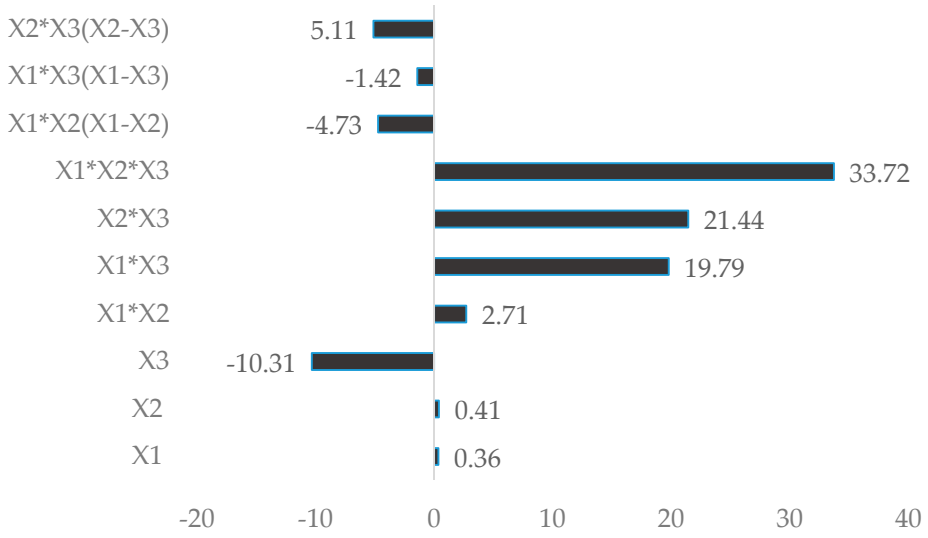

Figure 6. Contribution of factors to particle size.

This means that all of the binary effects and interactions between the three mixtures have a synergistic effect on the particle size. This can be due to the fact that the oil phase (sesame oil) and the emulsifying phase (soy lecithin/Tween) have in their composition high molecules, which are active molecules that have the ability to facilitate the formation of emulsions, improve their stability, and produce desirable properties in them [36]. In fact, high molecules adsorb to the surfaces of freshly formed oil droplets created by the homogenization of oil–water–molecules mixtures, where they facilitate further droplet disruption by lowering the interfacial tension and retard droplet coalescence by forming protective membranes around the droplets [37].

3.3.4. Optimization of Base Cream Formulation

In order to have a stable and optimal formulation, it is necessary to understand the proportion and nature of each component. In addition, each formulation must be specifically designed according to the desired purpose of its use and site of application. From the above observations, there must not be a high amount of oil phase (sesame oil) in the formulation to facilitate viscosity; instead, there should be a high amount of emulsifying phase (soy lecithin/tween) to maintain the emulsion. Thus, a multi-response analysis was done to obtain the optimal combination to be used to formulate the final product, with X_1:X_2:X_3 at a ratio of 24:28:10.

3.3.5. Microstructure Observation

Figure 7 shows the microstructures of the unhomogenised emulsion: sesame oil, *Aloe vera* gel, and soy lecithin/tween; and sesame oil, *Aloe vera* gel/gum, soy lecithin/Tween, and base cream.

We observed that when the aqueous phase is *Aloe vera* gel alone, the emulsion is not stabilized due to the fact that this gel loses its properties after extraction. A further reduction was observed with the addition of natural gum.

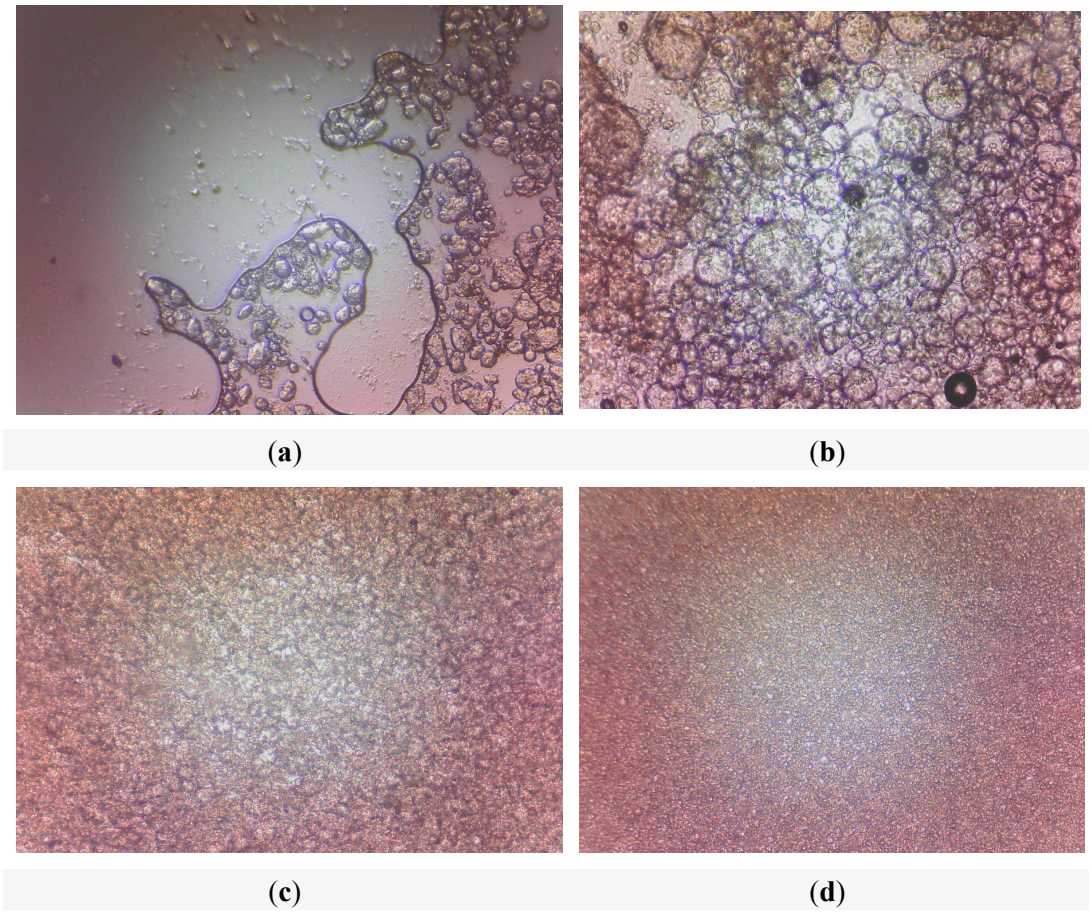

Figure 7. Microscopic images of (**a**) Unhomogenised emulsion; (**b**) Mixture of sesame oil, *Aloe vera* gel, and soy lecithin/tween; (**c**) Mixture of sesame oil, *Aloe vera* gel/gum, and soy lecithin/Tween; and (**d**) base cream.

4. Conclusions

This work aimed at studying the effect of local raw materials on a formulation of a topical cream emulsion. After screening, it was found that sesame oil, *Aloe vera* gel, and soy lecithin were the best ingredients for the cream emulsion. A multi-response optimization was done to obtain a combined optimal proportion, which gave us 24% of sesame oil, 28% of *Aloe vera* gel, and 10% of soy lecithin/Tween. However, studies still need to be done to determine the stability of the formulation in the long term and whether or not to use antimicrobial substances for the conservation of the formulation. This base cream can be used for further work as a matrix for the incorporation of the active principle in the cosmetic and pharmaceutical industries.

Acknowledgments: We thank the laboratories of University of Ngaoundere will provide the research facilities.

Author Contributions: Gertrude Eleonore DJIOBIE TCHIENOU, Roli Karole TSATSOP TSAGUE, Therese Florence MBAM PEGA, Vera BAMA, Albert BAMSECK, all make different formulations, and all analyses after the preparation of different emulsions. Gertrude Eleonore DJIOBIE TCHIENOU, Roli Karole TSATSOP TSAGUE, Selestin Dongmo SOKENG, and Martin Benoît NGASSOUM all interpret the results, write and corrected the article.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Vinod, P.; Shaha, A.Y.; Flavian, S.R.A.; Dalia, S.M.M.E. A science based approach to topical drug classification system (TCS). *Int. J. Pharm.* **2015**, *491*, 21–25.

2. Lucinda, B.; Richard, K.; Benjamin, W.; Anna, W.; John, S.; Chi, W.C.; Saleh, T.; Mamta, G.B.; Gil, J.K.; Arthur, K.; et al. Topical drug classification. *Int. J. Pharm.* **2005**, *295*, 101–112.
3. McClements, D.J. Reduced-fat foods: The complex science of developing diet-based strategies for tackling overweight and obesity. *Adv. Nutr.* **2015**, *6*, 338S–352S. [PubMed]
4. Cañizares, P.; Martínez, F.; Lobato, J.; Rodrigo, M.A. Break-up of oil-in-wateremulsions by electrochemical techniques. *J. Hazard. Mater.* **2007**, *145*, 233–240. [CrossRef] [PubMed]
5. Kralova, I.; Sjoblom, J. Surfactants used in food industry: A review. *J. Dispers. Sci. Technol.* **2009**, *30*, 63–83.
6. Damodaran, S. Protein stabilization of emulsions and foams. *J. Food Sci.* **2005**, *70*, 54–66.
7. Bouyer, E.; Mekhloufi, G.; Rosilio, V.; Grossiord, J.L.; Agnely, F. Proteins, polysaccharides, and their complexes used as stabilizers for emulsions: Alternatives to synthetic surfactants in the pharmaceutical field. *Int. J. Pharm.* **2012**, *436*, 359–378. [PubMed]
8. Baines, D.; Seal, R. *Natural Food Additives Ingredients and Flavourings*; Woodhead Publishing: Cambridge, UK, 2012.
9. Can, K.A.; Low, N.H.; Nickerson, M.T. Potential use of plant proteins in the micro-encapsulation of lipophilic materials in foods. *Trends Food Sci. Technol.* **2015**, *42*, 5–12.
10. Cheung, L.; Wanasundara, J.; Nickerson, M.T. Effect of pH and NaCl on the emulsifying properties of a napin protein isolate. *Food Biophys.* **2015**, *10*, 30–38.
11. Gilbert, L.; Picard, C.; Savary, G.; Grisel, M. Rheological and textural characterization of cosmetic emulsions containing natural and synthetic polymers: Relationships between both data. *Colloids Surf. A Physicochem. Eng. Asp.* **2013**, *421*, 150–163.
12. Silva, E.K.; Rosa, M.T.M.; Meireles, M.A.A. Ultrasound-assisted formation of emulsions stabilized by biopolymers. *Curr. Opin. Food Sci.* **2015**, *5*, 50–59. [CrossRef]
13. Alvarez-Lorenzo, C.; Blanco-Fernandez, B.; Puga, A.M.; Concheiro, A. Crosslinked ionic polysaccharides for stimuli-sensitive drug delivery. *Adv. Drug Deliv. Rev.* **2013**, *65*, 1148–1171. [CrossRef] [PubMed]
14. Tang, C.-H.; Yang, M.; Liu, F.; Chen, Z. A novel process to efficiently form transglutaminase-set soy protein isolate-stabilized emulsion gels. *LWT-Food Sci. Technol.* **2013**, *53*, 15–21. [CrossRef]
15. Rosa, M.; Kwiecien, M.; Tal-Figiel, B. Rheological investigations of pharmaceutical emulsions prepared with modified lecithin. *Czas. Tech.* **2013**. [CrossRef]
16. Kumar, R.; Katare, O.P. Lecithin organogels as a potential phospholipid-structured system for topical drug delivery: A review. *AAPS Pharm. Sci. Tech.* **2005**, *6*, E298–E310. [CrossRef] [PubMed]
17. Akpan, U.G.; Jimoh, A.; Mohammed, A.D. Extraction, Characterization and modification of castor seed oil. *Leonardo J. Sci.* **2006**, *8*, 43–52.
18. Narayan, P.; Shruti, S.; Priyam, S.; Debabrata, C.; Suaib, L.; Sudeep, T. Development and evaluation of *Aloe vera* (L.) Burm based topical cream formulation. *Ann. Phytomed.* **2014**, *3*, 60–65.
19. Peky, N.; Cristina, R.; Vladi, C.; Maria, T.; Elfriede, B.; Silvia, B. Optimization of *Pothomorphe umbellata* (L.) Miquel topical formulations using experimental design. *Int. J. Pharm.* **2008**, *353*, 149–159.
20. Evi-Maria, V.; Eforia, T.; Nikoleta, X.; Anna-Maria, D. Stability Study of O/W Cosmetic Emulsions Using Rosmarinus officinalis and Calendula officinalis Extracts. *Open J. Appl. Sci.* **2012**, *2*, 139–145.
21. Tsatsop, R.K.; Djiobie, G.; Regonne, K.; Bama, V.; Mbawala, A.; Ngassoum, M. Optimization of rheological properties in the formulation of an ointment base from natural ingredients. *Int. J. Sci. Technol. Res.* **2017**, *6*, 113–121.
22. Panda, P. Formulation and evaluation of topical dosage form of *Alangium salvifolium* linn. and their wound healing activity. *Asian J. Pharm. Sci. Res.* **2011**, *28*, 10–22.
23. Seamus, L.M.; Ruth, H.; Daniel, M. Effect of lecithin and monoglycerides on the heat stability of a model infant formula emulsion. *Food Hydrocolloids* **2008**, *22*, 888–898.
24. Shchipunov, Y.A.; Schmiedel, P. Phase behavior of lecithin at the oil/water interface. *Langmuir* **1996**, *12*, 6443–6445. [CrossRef]
25. Boyd, J.; Parkinson, C.; Sherman, P. Factors affecting emulsion stability, and the HLB concept. *J. Colloid Interface Sci.* **1972**, *41*, 359–370. [CrossRef]
26. Elleuch, M.; Besbes, S.; Roiseux, D.; Blecker, C.; Attia, H. Quality characteristics of sesame seeds and by-products. *Food Chem.* **2007**, *103*, 641–650. [CrossRef]

27. Rostami, M.; Farzaneh, V.; Boujmehrani, A.; Mohammadi, M.; Bakhshabadi, H. Optimizing the Extraction Process of Sesame Seed'S Oil Using Response Surface Method on the Industrial Scale. *Ind. Crops Prod.* **2014**, *58*, 160–165. [CrossRef]
28. Ilievska, B.; Loftsson, T.; Hjalmarsdottir, M.A.; Asgrimsdottir, G.M. Topical Formulation Comprising Fatty Acid Extract from Cod Liver Oil: Development, Evaluation and Stability Studies. *Mar. Drugs* **2016**, *14*, 105. [CrossRef] [PubMed]
29. Reiss, H. Entropy-induced dispersion of bulk liquids. *J. Colloid Interface Sci.* **1975**, *53*, 61–70. [CrossRef]
30. Baer, R.J.; Wolkow, M.D.; Kasperson, K.M. Effect of Emulsifiers on the Body and Texture of Low Fat Ice Cream. *J. Dairy Sci.* **1997**, *80*, 3123–3132. [CrossRef]
31. Gowda, D.C.; Neelisiddaiah, B.; Anjaneyalu, Y.V. Structural Studies of polysaccharides from *Aloe vera*. *Carbohydr. Res.* **1979**, *72*, 201–205.
32. Pattanayak, S.; Nayack, S.S.; Dinda, S.C.; Panda, K.; Naval, K.P. Evaluation of herbal ointments formulated with methanolic extract of *Cajanus scarabaeides*. *J. Pharm. Allied Health Sci.* **2011**, *1*, 47–59.
33. Pasupathi, A.; Palanisamy, P.; Jaykar, B.; Margret, C.; Venkateswarlu, B.S. Formulation, development, evaluation of calcitriol and clobetasol propionate ointment. *Indian J. Res. Pharm. Biotechnol.* **2013**, *1*, 95.
34. Amit, S.; Saraswati, B.; Kamalesh, U.; Kumud, U. Formulation and Evaluation of a Novel Herbal Gel of *Equisetum arvense* Extract. *J. Pharmacogn. Phytochem.* **2013**, *1*, 80–86.
35. Hamilton, R. Structure and general properties of mineral and vegetables oils used a spray adjuvant. *J. Pestic. Sci.* **1993**, *37*, 141–146. [CrossRef]
36. Quintana, S.E.; Franco, J.M.; Garcia-Zapateiro, L.A. Physicochemical and bromatological characteristics of arenca (*Triportheus magdalenae*), and rheological properties of oil-in-water emulsions containing isolated protein. *Ciênc. Agrotecnol.* **2015**, *39*, 634–641. [CrossRef]
37. Walstra, P. *Physical Chemistry of Foods*; Marcel Decker: New York, NY, USA, 2003.