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Characterization studies of Nanoemulsion and Nanoemulgel Formulations

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DECLARATION

I hereby declare that this thesis entitled "Characteristic studies of Nanoemulsion and Nanoemulgel Formulations" is the result of my own research except as cited in the references.

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Characterization studies of Nanoemulsion and Nanoemulgel Formulations

ABSTRACT

This research aims to provide formulations for nanoemulsion and nanoemulgel, and to determine the characteristics of each utilized formulation. Nanoemulsion formulations were obtained from the ternary phase diagram involving distilled water, soybean oil, and surfactants (Tween 80 and glycerol) based on previous research. The nanoemulsion consists of 60% Tween 80 + glycerol, 30% water, and 10% soybean oil. Nanoemulsion was prepared using the low-energy emulsification method or spontaneous emulsification method. All tests were conducted to assess the characteristics of both nanoemulsion and nanoemulgel. Nanoemulgel was obtained by combining nanoemulsion with Carbopol 940 as a gelling agent. Different formulations of nanoemulsion were prepared based on the ternary phase diagram. These characteristics were also studied to determine the effectiveness differences between nanoemulsion and nanoemulgel. This is due to the use of ten different formulas based on points on the ternary phase diagram and variations in the amount of Carbopol 940 used in the nanoemulsion to form a perfect nanoemulgel. To create a stable nanoemulsion and nanomugel, we subsequently analyzed their characteristics. The characterization of the nanoemulsion and nanoemulgel involved assessing their appearance, pH levels, stability, viscosity, and Tyndall effect. Results revealed that nanoemulsion and nanoemulgel formulations were stable, displaying no separation. The pH measurements indicated that the solution was acidic and not suitable for the skin. The Tyndall effect confirmed the classification of all formulations as nanoemulsions, macroemulsions, and microemulsions. Viscosity measurements enabled researchers to comprehend the relative thickness of each nanoemulgel formulation in the result comparison. The spreadability resulted in the conclusion that the concentration of nanoemulsion in the nanoemulgel formulation significantly influenced the spreadability of the final product and highlighting the importance of formulation in product development.

Keywords: Nanoemulsion, Nanoemulgel, Features, ternary phase diagrams.

Kajian pencirian Nanoemulsion dan Formulasi Nanoemulgel

ABSTRAK

Penyelidikan ini bertujuan untuk menyediakan formulasi untuk nanoemulsion dan nanoemulgel, dan untuk menentukan ciri-ciri setiap formulasi yang digunakan. Formulasi nanoemulsion diperolehi daripada rajah fasa ternari yang melibatkan air suling, minyak kacang soya, dan surfaktan (Tween 80 dan gliserol) berdasarkan penyelidikan terdahulu. Nanoemulsion terdiri daripada 60% Tween 80 + gliserol, 30% air, dan 10% minyak kacang soya. Nanoemulsion disediakan menggunakan kaedah emulsifikasi tenaga rendah atau kaedah emulsifikasi spontan. Semua ujian telah dijalankan untuk menilai ciri-ciri kedua-dua nanoemulsion dan nanoemulgel. Nanoemulgel diperolehi dengan menggabungkan nanoemulsion dengan Carbopol 940 sebagai agen gelling. Formulasi nanoemulsion yang berbeza disediakan berdasarkan rajah fasa ternary. Ciri-ciri ini juga dikaji untuk menentukan perbezaan keberkesanan antara nanoemulsion dan nanoemulgel. Ini disebabkan oleh penggunaan sepuluh formula yang berbeza berdasarkan titik pada rajah fasa ternari dan variasi dalam jumlah Carbopol 940 yang digunakan dalam nanoemulsion untuk membentuk nanoemulgel yang sempurna. Untuk mencipta nanoemulsion dan nanomugel yang stabil, kami kemudiannya menganalisis ciri-ciri mereka. Pencirian nanoemulsion dan nanoemulgel melibatkan menilai penampilan mereka, tahap pH, kestabilan, kelikatan, dan kesan Tyndall. Keputusan menunjukkan bahawa formulasi nanoemulsion dan nanoemulgel stabil, tidak memaparkan pemisahan. Pengukuran pH menunjukkan bahawa penyelesaiannya berasid dan tidak sesuai untuk kulit. Kesan Tyndall mengesahkan klasifikasi semua formulasi sebagai nanoemulsions, macroemulsions, dan microemulsions. Pengukuran kelikatan membolehkan penyelidik memahami ketebalan relatif setiap formulasi nanoemulgel dalam perbandingan hasil. Kebolehbaran mengakibatkan kesimpulan bahawa kepekatan nanoemulsion dalam formulasi nanoemulgel sangat mempengaruhi penyebaran produk akhir dan menonjolkan kepentingan formulasi dalam pembangunan produk.

Kata kunci: Nanoemulsion, Nanoemulgel, Ciri-ciri, gambar rajah fasa ternari.

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LIST OF ABBREVIATIONS

(o/w)	Oil-in-Water	20
(w/o)	Water-in-Oil	20
pH	measure of how acidic/basic water	24
Rpm	Revolutions per minute	26
Kg	Kilogram	28
g	gram	29
ml	milimeter	43
SD	Standard Deviation	53

LIST OF SYMBOLS

mPa•s	millipascal-second	28
%	Percentage	28
±	plus-minus	46

CHAPTER 1

INTRODUCTION

1.1 Background of Study

Previously, the implementation of nanotechnology in the domain of health science was a source of significant advancements and opportunities. Researchers and scientists actively explored and harnessed the potential of nanotechnology to transform healthcare in various ways. Nanoemulsions were thermodynamically stable colloidal dispersion systems made of two immiscible liquids combined with a surfactant and cosurfactant to produce a single phase (Gupreet K. et al. 2018). Nasal-scale drug delivery systems that had nano-sized particles or molecules increased drug solubility and permeability due to nano oil droplets that provided a larger surface area for drug liberation and faster absorption from biological barriers, and this led to increased bioavailability for both hydrophilic drugs and hydrophobic drugs, increasing the therapeutic effectiveness of drugs (Patra et al., 2018). Furthermore, the same research article aimed to consolidate nanoemulsion formulation and characterization methods.

In the past, Nanoemulsion and nanoemulgel were both applications of nanotechnology in the field of drug delivery, specifically in the topical route. While they shared similarities, they had distinct characteristics and advantages. Nanoemulgel was able to deliver lipophilic

medicines topically (Azeez & Alkotaji, 2021). Nano-emulgels gained attention due to their targeted distribution, convenience of use, lack of gastrointestinal degradation or first-pass metabolism, and safety (Mahipal Reddy Donthi et al. 2023). Therefore, they had characterization differences that made them have different delivery systems.

In this context, a comparison was conducted to distinguish the characterization of nanoemulgel from that of nanoemulsion. It was suggested that laboratory tests be employed instead of fieldwork tests, as the former relied on characterization experiments and necessitated skilled use of research equipment in a controlled laboratory setting.

1.2 Problem Statement

Nanoemulsion and nanoemulgel were two different formulations used in topical drug delivery, each offering unique characteristics and advantages. However, an understanding of all the differences between the systems was important to determine the appropriateness of useComparative data on stability, drug delivery capacity, and formulation were lacking at the time. This knowledge prevented researchers or users from making decisions when choosing the appropriate formulation for topical drug delivery between the two nanoemulsions and nanoemulgels. Therefore, there was a need to conduct a comprehensive study comparing nanoemulsions and nanoemulgels to clarify their differences in terms of their characterization. Such studies would provide valuable insight into the advantages and limitations of these formulations, allowing clearer information to optimize topical drug delivery systems and their effective and efficient use in pharmaceutical and cosmetic applications.

1.3 Objective

The objectives of this study are:

1. To develop nanoemulsions and nanoemulgels formulation.
2. To study characterization of nanoemulsion and nanoemulgel.

1.4 Scope of study

The objective of the study was to encompass the characterization and comparative analysis of nanoemulsions and nanoemulgels designed for topical drug delivery. During the initial phase of the research, emphasis was placed on characterizing the physical and chemical properties of both nanoemulsions and nanoemulgels. This involved investigating aspects such as appearance, viscosity, stability, pH measurement, and spreadability. In the next stage, the characterization differences between nanoemulgel and nanoemulsion were explained. The study compared the characterization of nanoemulsions and nanoemulgels and analyzed the differences in the physical and chemical properties of nanoemulsions and nanoemulgels. The focus was given to identifying characterization differences.

1.6 Significant of Study

The results of this study provided characterization and comparative analysis of nanoemulsion and nanoemulgel. By comparing the characteristics and performance of nanoemulsion and nanoemulgel, this study helped researchers and users understand the differences between nanoemulsion and nanoemulgel formulations and provided a reference for

selecting a specific drug delivery system. The study contributed to the technological advancement of the diffusion profile and depth of drug penetration from nanoemulsion and nanoemulgel formulations. The obtained information could be used to design and optimize new drug delivery systems, leading to more targeted and efficient drug delivery.

CHAPTER 2

LITERATURE REVIEW

2.1 Nanoetecnology

Nanotechnology was the manipulation of matter at the atomic level to make new structures, materials, and nanometers. These things had their own qualities that changed how they acted. However, we didn't yet know everything there was to know about the health risks of working with nanomaterials (Bhushan, 2017). Workers in businesses linked to nanotechnology could be exposed to manufactured materials with new qualities, but there wasn't much known about how they were exposed, how harmful they were, or how much contact was safe. Research showed that nanoparticles with low solubility were more poisonous than bigger particles, and that their surface area and chemistry played a big role in how living things reacted to them. The Centers for Disease Control and Prevention (CDC) found that some nanoparticles moved from the breathing system to other areas (Kulinowski & Lippy, 2011). Nanotechnology, which worked with materials on the nanoscale (1–100 nanometers), was used more and more in many areas of life, including health. Due to their small size, nanomaterials had unique qualities, such as being highly reactive and able to put themselves together. But there were worries about how dangerous they might be. Nanotechnology gave lung medicine new ways to treat diseases, but it also raised questions about how particles affected the respiratory system. To use nanotechnology in lung

medicine successfully, one had to understand these benefits and ensure it was safe (Omlor et al. 2015).

2.2 Nanoemulsion

Nanoemulsions were tiny drops of one liquid that were spread out in another liquid that they couldn't mix with. Extreme emulsification methods, such as microfluidic and acoustic techniques, were used to make these nanoemulsions by breaking bigger drops into smaller ones. A stabilizing detergent kept the nanoemulsion steady over a long period of time by stopping droplets from coming together (Mason, Wilking, K. Meleson, Chang, & Graves, 2017). Nanoemulsions were made up of tiny drops that were spread out in a continuous phase. Nanoemulsions had many benefits over oil-in-water (o/w) emulsions because the droplets were so small. Nanoemulsions had drops that were between 20 and 200 nanometers in width. This gave them a big surface area, which improved their qualities and efficiency. These included high kinetic stability, low viscosity, transparency or translucency, high solubilization capacity, low surfactant consumption, and security of contained active chemicals. Nanoemulsions could be made through high-energy processes like high-pressure homogenization and sonication, or through low-energy processes like phase inversion. The goal of ongoing study and new ideas was to improve the qualities of nanoemulsions by working on ways to improve droplet size control, stability, and controlled release. Nanoemulsions were made up of tiny drops that were spread out in a continuous phase. Nanoemulsions had many benefits over oil-in-water (o/w) emulsions because the droplets were so small. Nanoemulsions had drops that were between 20 and 200 nanometers in width. This gave them a big surface area, which improved their qualities and efficiency. These included high kinetic stability, low viscosity, transparency or translucency, high

solubilization capacity, low surfactant consumption, and security of contained active chemicals. Nanoemulsions could be made through high-energy processes like high-pressure homogenization and sonication, or through low-energy processes like phase inversion. The goal of ongoing study and new ideas was to improve the qualities of nanoemulsions by working on ways to improve droplet size control, stability, and controlled release (Chuo & Mohd Setapar, 2022).

Figure 2.1: Nanoemulsions (o/w) or (w/o) (Ashaolu, 2021).

Nanoemulsions were rated based on their entrapment efficiency, particle size, polydispersity index, and zeta potential. Nanoemulsions were studied by transmission electron microscopy, Fourier transform infrared spectroscopy, and differential scanning calorimetry. Pharmaceutical properties such as solubility, dispersibility, viscosity, surface tension, fricohesity, refractive index, percent distribution, pH, and osmolarity were investigated in vitro (Teo Chai Ting et al., 2020).

Topical drug delivery had many benefits, such as the patient's willingness to use it, the fact that it didn't cause pain, and its localized action. It bypassed the first-pass metabolism in the liver, facilitated easier drug absorption through the skin, and potentially enhanced drug bioavailability. Nanoemulsion was a stable mixture of oil and water with droplets sized in nanometers. However, its low viscosity made it difficult to spread and adhere to the skin. To

overcome this issue, nanoemulsions could be incorporated into gel formulations to create nanoemulgels. Nanoemulgels combined the advantages of both methods, allowing for improved drug absorption through the skin, increased drug loading, reduced discomfort, and better spreadability. They had applications in local, systemic, and brain-blood barrier drug delivery. Nanoemulgels exhibited greater stability and more controlled drug release compared to regular emulgels. They were extensively studied in experimental and clinical settings for the treatment of various skin diseases and conditions. Some nanoemulgels were already available on the market, and ongoing research aimed to assess their efficacy (Hartmann, 2023).

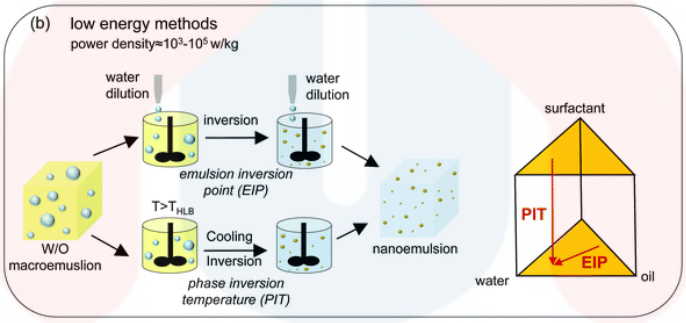

Figure 2.2: Nanoemulsions (o/w) or (w/o)

(Ashaolu, 2021).

2.3 Nanoemulgel

Nanoemulgel is basically an emulsion-based topical gel formulation, where nanosized emulsion globules can be prepared with the help of high energy or low energy methods and further converted into nanoemulgel by adding a suitable gelling agent. Nanoemulgel fabrication enlists various kinds of polymeric materials, surfactants and fatty substances of natural, synthetic and semi-synthetic nature with a globule size range from 5 to 500 nm (Anand et al., 2019).

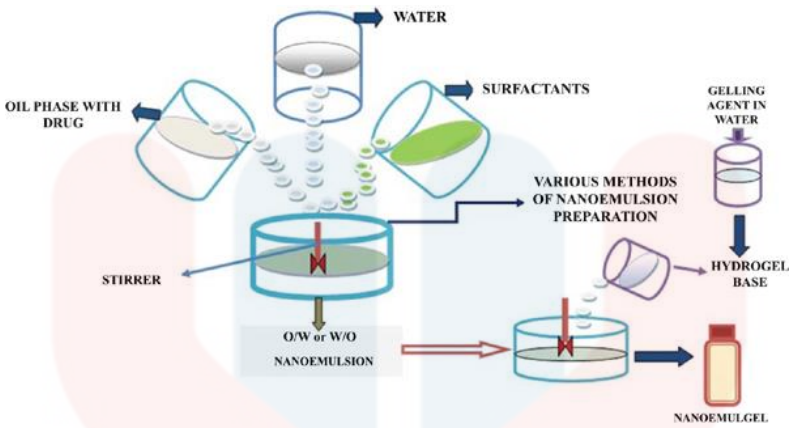

Figure 2.3: Nanoemulgel preparations (Anand et al., 2019).

Nanoemulgels were a type of drug delivery system that combined the good qualities of nanoemulsions and gels. They had a lot of promise in the field of pharmaceutical research. Nanoemulsions were made up of small oil drops spread out in a liquid medium. They were good carriers for lipophilic drugs as they made them more soluble, stable, and bioavailable. They also had better porosity, making them suitable for various drug administration routes. When drugs were incorporated into nanoemulgel devices, several benefits were observed (Aithal, Narayan, & Nayak, 2020).

Nano-emulgel is an emerging drug delivery system intended to enhance the therapeutic profile of lipophilic drugs. Lipophilic formulations have a variety of limitations, which includes poor solubility, unpredictable absorption, and low oral bioavailability. Nano-emulgel, an amalgamated preparation of different systems aims to deal with these limitations. The novel system prepared by the incorporation of nano-emulsion into gel improves stability and enables drug delivery for both immediate and controlled release (Indriati et al., 2018).

The structure of nanoemulgels also allowed for the slow and sustained release of drugs over an extended period. This characteristic was particularly beneficial when maintaining a fixed drug dosage was crucial for treatment effectiveness (Aithal, Narayan, & Nayak, 2020).

2.5 Characteristics Test

2.5.1 Appearance Test

Nanoemulgel had a smooth, translucent, semi-solid texture. Its glossy surface mimicked that of a gel. Depending on the concentration of emulsion droplets, nanoemulgels could appear semi-translucent or milky. This formulation utilized a gel-like matrix with nanosized emulsion droplets measuring fewer than 100 nanometers in diameter. Nanoemulsion was translucent or transparent and could appear milky or hazy. Its homogeneous dispersion of nanosized oil droplets in a continuous aqueous phase made it attractive and stable (Aithal, Narayan, & Nayak, 2020).

2.5.2 Viscocity

Nanoemulsion physicochemical characterization required viscosity measurement. The Ostwald, Hoeppler falling ball, Stormer, Brookfield, and Ferranti-Shirley viscometers were used to measure viscosity. Nanoemulsion viscosity was often measured using the Brookfield viscometer. Low viscosity indicated oil-in-water emulsions, while high viscosity indicated water-in-oil systems. The survismeter, which measured nanoemulsion parameters such as surface tension, viscosity, interfacial tension, contact angle, dipole moment, particle size, and

hydrodynamic volumes, was also commonly used. Shafiq et al. used a Brookfield cone and plate rheometer to measure the viscosity of ramipril nanoemulsion formulations, which ranged from 10.68 to 21 cP (Gurpreet & Singh, 2018).

2.5.3 Stability

Stability studies determined nanoemulsion stability. These investigations assessed medication stability under temperature, humidity, and light. Nanoemulsion stability experiments followed International Conference on Harmonisation (ICH) requirements and comprised 24 months of dispersion and freeze-dried storage. Nanoemulsions were tested at ambient, refrigeration, and freezing conditions. Samples were taken at set times and analyzed for particle size, drug loading, encapsulation effectiveness, and in vitro drug release profile (Gurpreet & Singh, 2018).

2.5.4 ph measurement

A digital pH meter checked nanoemulgel skin compatibility. The typical pH of the skin was generally around 6-7. The pH value indicated the acidity or alkalinity of the nanoemulgel. An alkaline pH could potentially irritate and disrupt the skin, while acidic skin could also cause irritation. Digital pH meters were known for their accuracy in measuring pH. A pH electrode was used to measure hydrogen ions and determine the pH of the nanoemulgel. Adjustments to the pH of the nanoemulgel could be made by adding acids or bases. For lowering the pH, citric or lactic acid could be added, while bases such as sodium hydroxide or triethanolamine were used to elevate the pH (Ren et al., 2021).

2.5.5 Spreadability Test

The viscosity of the nanoemulgel affected the spreadability of a topical dose. Spreadability played a crucial role in providing a consistent dose and improving effectiveness by ensuring even distribution of the dosage form. The spreadability was approximated through the parallel-plate approach and human subject evaluation. The parallel-plate approach, also known as the slide and drag method, was widely utilized due to its simplicity and low cost. The spreadability of the dosage form was measured using two glass slides, one stationary and one mobile. A specific calculation based on the time required for sliding off was used to determine the spreadability (Mahipal Reddy Donthi et al., 2023).

2.5.6 Tyndall Effect test

The Tyndall effect or Tyndall scattering is the scattering of light by small, suspended particles in a colloid or fine suspension, making the light beam visible. For example, the beam of a flashlight is visible when you shine it through a glass of milk (a colloid). The effect takes its name for 19th century physicist John Tyndall, who first described and studied the phenomenon (Helmenstine, 2022).

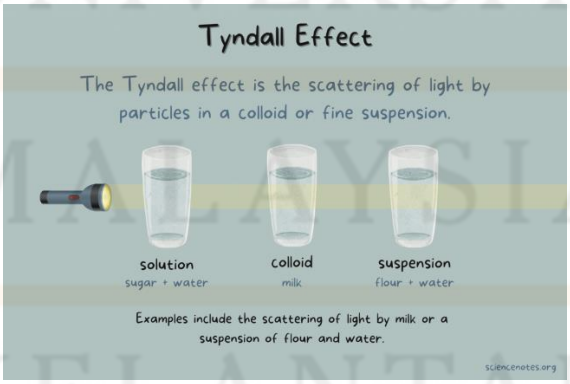

Figure 2.4: Tyndall Effect

(Helmenstine, 2022)

The Tyndall effect distinguished colloids from true chemical solutions. The particles in a solution were very small, while those in a colloid ranged from 1 to 1000 nanometers in diameter. So, if a flashlight beam was shone into a glass of sugar water or salt water (solutions), the beam was not visible. However, the beam was visible in a glass of skim milk or container of gelatin (colloids). The Tyndall effect also produced scattering in fine suspensions, such as a mixture of flour and water. However, the particles in a suspension eventually settled out, while those in a colloid remained homogeneous (Helmenstine, 2022).

CHAPTER 3

MATERIALS AND METHODS

3.1 Material

Oil, water, detergent, and a gel-forming substance were sourced from the UMK laboratory. Tween 80, glycerol, and soybean oil were used to prepare nanoemulsion formulation. Distilled water prepared by the laboratory was used during steam distillation process and the preparation of nanoemulsion. The magnetic stirrer used was provided by the laboratory The vials used to keep nanoemulsion formulation. Carbopol 940 were used to prepared the nanoemulgel formulation produced by the laboratory.

3.2 Method

3.2.1 Nanoemulsion Formulation

A stable concentrated nanoemulsion was prepared using the pseudo-ternary diagram constructed by Ziheng Wang (2009). The nanoemulsion was formed by mixing glycerol and Tween 80 with soybean oil as the dispersed phase, while distilled water served as the dispersing medium. The mixing process was carried out using a magnetic stirrer at a speed of 400 rpm to obtain a stable concentration of nanoemulsion.

To produce the nanoemulsionIn, the process 1.5 ml of the concentrated nanoemulsion was combined with 50 ml of distilled water. The stable region of the oil-in-water nanoemulsion was visually depicted by shading the relevant area on the constructed pseudo-ternary phase

diagram, as shown in Figure 3.1. Each corner of the phase diagram represented 100% concentration of the respective constituent.

Table 3.1 Formulation of points plotted on the ternary phase diagram.

Point	Water (g)	Oil phase (Soybean oil) (g)	Surfactan (Tween80) (g)	Co-surfactant (glycerol) (g)
F1	0.60	1.80	3.80	3.80
F2	1.20	1.60	3.60	3.60
F3	1.80	1.40	3.40	3.40
F4	2.40	1.20	3.20	3.20
F5	3.00	1.00	3.00	3.00
F6	3.60	0.80	2.80	2.80
F7	4.20	0.60	2.60	2.60
F8	4.80	0.40	2.20	2.20
F9	5.40	0.20	2.20	2.20
F10	5.90	0.10	2.00	2.00

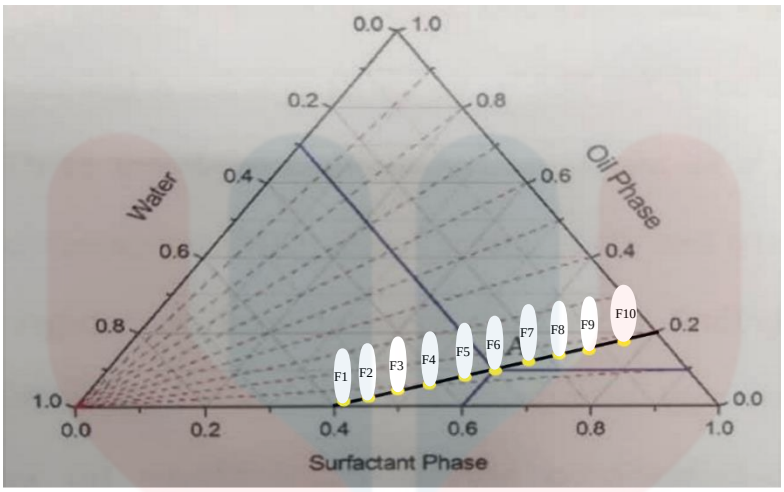

Figure 3.1: The ternary phase diagram for the system containing water, soybean oil, Tween 80, and glycerol. Point F1, F2, F3, F4, F5, F6, F7, F8, F9, and F10 plotted on a triangular graph to find those that produced nanoemulsion.

3.2.3 Nanoemulgel formulation

The nanoemulgel was formed by gently stirring a 1:1 volume ratio of the prepared nanoemulsion and the gel base, employing a stir rod in the process. The gel base was prepared by mixing through the nanoemulsion formulation. The amount of Carbopol added to the nanoemulsion formulation was varied into 5%, 10%, and 15%. Lastly, the nanoemulsion formulation was formed as a nanoemulgel. Other nanoemulgels were obtained by mixing the prepared concentration nanoemulsion formulation, which was F5 (3331). The amount of Carbopol added to its formulation was varied into 5%, 10%, and 15%.

3.2.5 Characteristic studies

3.2.5.1 Appearance

The visual characteristics of both nanoemulsion and nanoemulgel were examined and contrasted with the physical appearance of macroemulsion, nanosemulsion, and microemulsion, which were charted on the ternary phase diagram for comparison. The appearance test involved visually inspecting and analyzing the formulations to assess their macroscopic characteristics, such as color, transparency, and texture.

3.2.5.2 Viscocity

The vibro viscometer test of nanoemulgel and nanoemulsion was conducted by evenly inserting the samples into the vibro viscometer sensor plate. The viscosity measurement was initiated by starting the vibration at a predetermined frequency, and the viscosity data was recorded for a relevant period of time to observe the viscosity changes in the nanoemulgel or nanoemulsion. Viscosity during thixotropic processes, such as stirring or application, was observed, and changes in viscosity response were noted to understand the thixotropic properties of both formulations. Vibro viscometer testing provided significant insight into the past viscosity, durability, and thixotropic properties of nanoemulgels and nanoemulsions. Unit "mPa•s" was used as the unit of measurement for the displayed value of the SV-A Series. If the sample density was not 1 [kg/m3], the absolute viscosity value could be obtained by dividing the displayed value by the sample density.

3.2.5.3 Stability

A stability test was conducted by observing all the samples of nanoemulsion and nanoemulgel at room temperature over a 14-day period. The objective of the stability test was to determine the duration at which nanoemulsion and nanoemulgel lost their stability, as assessed through visual observations on each sample. Stability studies are performed for assessing the stability of the drug substance under the influence of various environmental factors like temperature, humidity and light (Mulia et al., 2018).

3.2.5.4 ph measurement

The pH measurement was conducted using a digital pH meter to assess all nanoemulsion and nanoemulgel formulations. The pH of the samples was expected to be around 6-7 to align with the optimal skin condition.

3.2.5.5 Spreadability Test

The spreadability of various nanoemulgel formulations was assessed by measuring the spreading diameter of 0.5 g of each sample between two horizontal glass plates after one minute. A 5g weight was subsequently applied to the upper plate. Each formulation underwent three determinations to ensure the accuracy and consistency of the results.

3.2.5.6 Tyndall effect

Tyndall effect was done on water, macroemulsion and nanoemulsion. A laser was pointed at the solution that was going to be observed. A conical light beam generated from the scattering of light by colloidal particles.

CHAPTER 4

RESULT AND DISCUSSION

4.1 Nanoemulsion and Nanoemulgel Formulation and Formation

4.1.1 Nanoemulsion Formulation and Formation

Four materials are used to produce the nanoemulsion: water, soybean oil, co-surfactant (glycerol) and surfactant (Tween 80). To determine the point at which a nanoemulsion will develop, ten points—F1, F2, F3, F4, F5, F6, F7, F8, F9, and F10—were plotted on the tetary phase diagram, as seen in Figure 4.1. They are all examined closely, and each sample's physical attributes are compared with them. Table 4.1 presents each plot point in summary form. The nanoemulsion formulation obtained in this research was based on the ternary phase diagram constrcuted by Wang (2009).

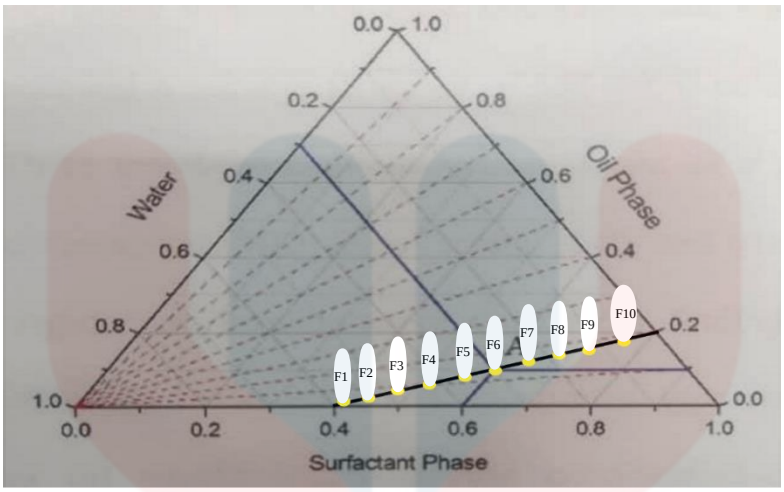

Figure 4.1: The pseudo ternary phase diagran. Point F1, F2, F3, F4, F5, F6, F7, F8, F9, and F10 are plotted to find those that produce nanoemulsion.

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F3	1.80	1.40	3.40	3.40
F4	2.40	1.20	3.20	3.20
F5	3.00	1.00	3.00	3.00
F6	3.60	0.80	2.80	2.80
F7	4.20	0.60	2.60	2.60
F8	4.80	0.40	2.20	2.20
F9	5.40	0.20	2.20	2.20
F10	5.90	0.10	2.00	2.00

The formation of nanoemulsion begins by adding the surfactant and co-surfactant at a ratio of 1:1 on a weight basis. Point F5, with 30% water, 60% surfactant, and 10% soybean oil was done first because it was proven in the previous research to be able to achieve nanoemulsion (Z. Wang, 2009). 10 milliliters of beaker were used to combine 3.0 g of Tween 80, 3.0 g of glycerol, and 1.0 g of soybean oil. A stirrer was used to agitate the mixture on a magnetic stirrer with a speed of 400 rpm. The mixture was gradually supplemented with 3.0 ml distilled water drop by drop. The assembly was then referred to as a concentration when all the parts had been put together. Figure 4.1 showed the formulation points plotted on the ternary phase diagram.

Figure 4.2: The concentrates of formulation of point F1, F2, F3, F4, F5, F6, F7, F8, F9, and F10 (from left to right).

The final nanoemulsion was made by diluting 1.5 ml of the concentrate in 50 ml of distilled water. Nanoemulsion was obtained when the dilution turns into a bluish transparent solution, which could be caused by the tyndall effect (Ostrosky, Rocha-filho, & Verissimo, 2015). Similar to the first sample, the other samples were white, homogeneous, and fluid in appearance.

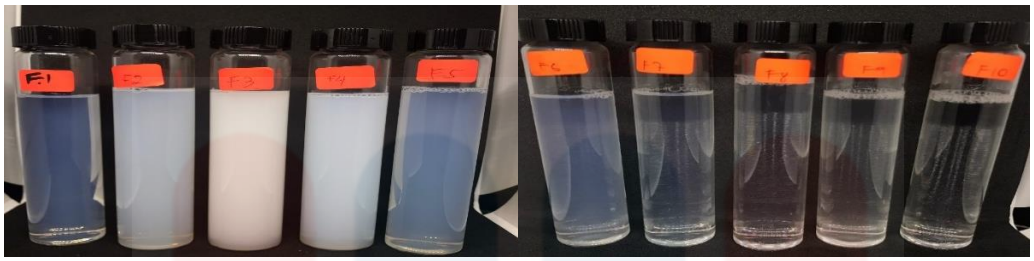


Figure 4.3: Dilution of point F1, F2, F3, F4, F5, F6, F7, F8, F9, and F10 (from left to right).

The shematic depiction of the dilution process used to create the nanoemulsion is shown in Figure 4.4 Concentrated emulsion (left) was found in the bicontinuous zone. Nanoemulsion was the result of diluting a significant volume of water with tiny droplets that were nanosized. According to Fernandez, Rieger & Angelika, (2004) the nanoemulsion would be produced within the bicontinuous phase when there is an unspectacular change in the environmental condition.

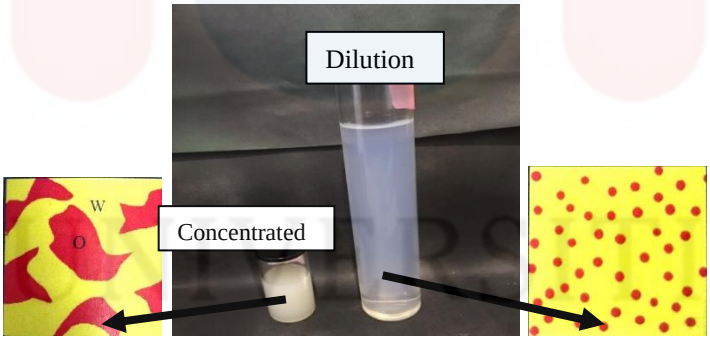


Figure 4.4: The schematic representation of the dilution process to produce nanoemulsion.

4.1.2 Nanoemulsion Formulation mixed with Carbopol 940

Table 4. 2 Nanoemulsion sample that mixed with Carbopol 940.

Carbopol 940	Nanoemulgel									
5%	Ng1.1	Ng2.1	Ng3.1	Ng4.1	Ng5.1	Ng6.1	Ng7.1	Ng8.1	Ng9.1	Ng10.1
10%	Ng1.2	Ng2.2	Ng3.2	Ng4.2	Ng5.2	Ng6.2	Ng7.2	Ng8.2	Ng9.2	Ng10.2
15%	Ng1.3	Ng2.3	Ng3.3	Ng4.3	Ng5.3	Ng6.3	Ng7.3	Ng8.3	Ng9.3	Ng10.3

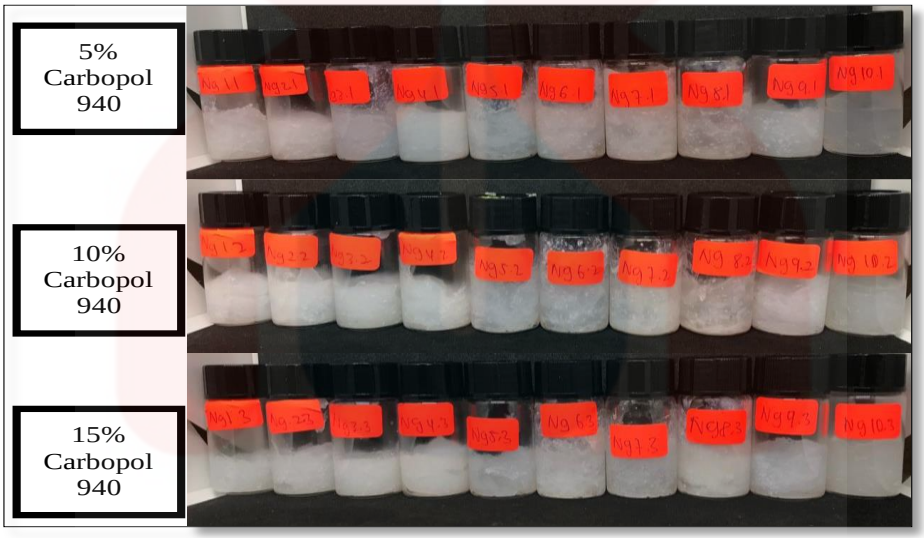


Figure 4.5: Nanoemulsion sample that mixed with Carbopol 940.

Table 4.5 showed the nanoemulsion samples that were combined with Carbopol 940 at different concentrations. Because carbopol 940 is a stabilizing and thickening polymer, it is often used in pharmaceutical and cosmetic formulations. A systematic overview of Nanoemulgel formulations at three different Carbopol 940 concentrations (5%, 10%, and 15%) is provided in the table. The nanoemulgel samples are labeled Ng1.1 to Ng10.1 for the 5% Carbopol 940 concentration, Ng1.2 to Ng10.2 for the 10% concentration, and Ng1.3 to Ng10.3 for the 15%

concentration. A column is used to represent each Nanoemulsion sample under the relevant Carbopol concentration. For instance, Ng1.1 represents the first Nanoemulsion sample at a Carbopol 940 concentration of 5%, Ng2.1 represents the second sample, and so on. A similar pattern is seen for the Carbopol 940 concentrations of 10% and 15%.

4.1.3 Nanoemulsion from nanoemulgel 5%, 10% and 15%

Table 4.3 Making nanoemulsion from nanoemulgel with 5%, 10%, 15% of Carbopol 940.

Carbopol 940	**Nanoemulsion from Nanoemulgel**									
5%	Gn1.1	Gn2.1	Gn3.1	Gn4.1	Gn5.1	Gn6.1	Gn7.1	Gn8.1	Gn9.1	Gn10.1
10%	Gn1.2	Gn2.2	Gn3.2	Gn4.2	Gn5.2	Gn6.2	Gn7.2	Gn8.2	Gn9.2	Gn10.2
15%	Gn1.3	Gn2.3	Gn3.3	Gn4.3	Gn5.3	Gn6.3	Gn7.3	Gn8.3	Gn9.3	Gn10.3

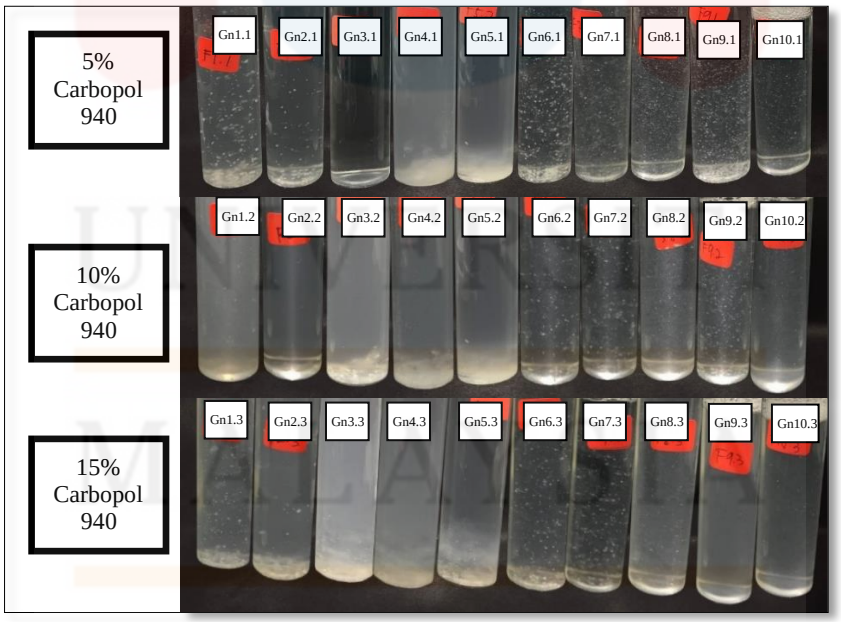


Figure 4. 6: Nanoemulsion sample from nanoemulgel 5%, 10% and 15%.

The nanoemulsion samples were mixed at varying doses with Carbopol 940, as shown in Table 4.2. Table 4.3 provided an extensive overview of the nanoemulsion formulations produced using three distinct nanoemulgel concentrations: 5%, 10%, and 15%. Samples of nanoemulsion at a concentration of 5% nanoemulgel were labeled with Gn1.1 to Gn10.1, samples at a concentration of 10% nanoemulgel were labeled with Gn1.2 up to Gn10.2, and samples at a concentration of 15% nanoemulgel were labeled with Gn1.3 up to 10.3.

4.1.4 Nanoemulgel Formulation F5 (3331)

Table 4.4 Nanoemulgel from Nanoemulsion formulation F5 (3331).

Carbopol 940	**Nanoemulgel F5 (3331)**
5%	Fg1
10%	Fg2
15%	Fg3

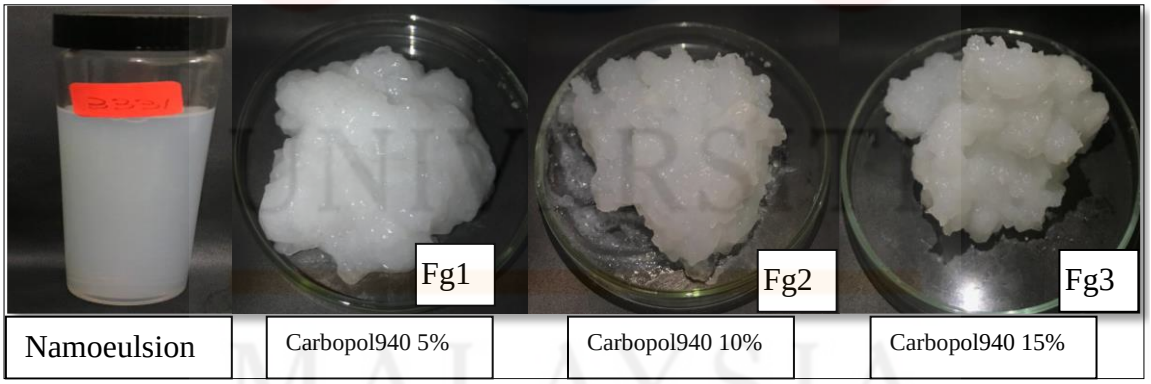


Figure 4.7: Nanoemulgel Gg1, Fg2 and Fg3 from Nanoemulsion formulation F5 (3331).

Table 4.4 and Figure 4.7 represented the formulation of Nanoemulgel obtained from Nanoemulsion Formulation 3331 (F5) with varying concentrations of Carbopol 940 (5%, 10%,

and 15%). Each row corresponded to a specific Carbopol concentration, and the resulting Nanoemulgel formulations were denoted as Fg1 for 5%, Fg2 for 10%, and Fg3 for 15%.

4.1.5 Nanoemulgel from Concentrated Formulation F5 (3331)

Table 4.5 Nanoemulgel Neg5, Neg10 and Neg15 from concentrated F5 (3331).

Carbopol 940	**Concentrated Formulation F5 (3331)**
5%	Neg5
10%	Neg10
15%	Neg15

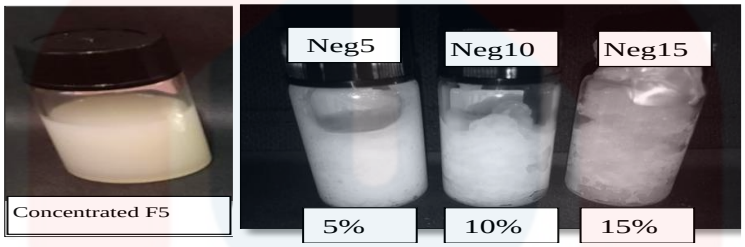


Figure 4.8 : Nanoemulgel Neg5, Neg10 and Neg15 from concentrated F5 (3331).

Table 4.5 outlined the formulations of Nanoemulgel Neg5, Neg10, and Neg15, derived from Concentrated Formulation F5 (3331), with varying concentrations of Carbopol 940 (5%, 10%, and 15%). Accompanying this table was Figure 4.5, which likely visualized or graphically represented aspects of Nanoemulgel Neg5, Neg10, and Neg15 from Concentrated Formulation F5 (3331)

4.2 Nanoemulsion, Macroemulsion and Nanoemulgel Samples Test

4.2.1 Physical Appearance Test of Nanoemulgel, Macroemulsion dan Nanoemulsion

The physical appearance test was conducted on nanoemulgel, water, macroemulsion, and nanoemulsion to observe their differences in appearance. The results were presented in Table 4.2.1 based on visual observations.

Table 4.6 the physical appearance of differences between water, macroemulsion, and nanoemulsion

Solution	**Water**	**Macroemulsion**	**Nanoemulsion**	**Nanoemulgel**
Colour	Clear	White/milk	Bluish/Cloudy	Clear White
Transparency	Scattering	Opaque	Transparent	Opaque

Table 4.7 Nanoemulsion Formulation appearance

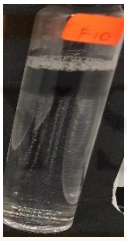
	F1 Bluish/cloudy		F6 Bluish/cloudy
	F2 Bluish/cloudy		F7 White Clear
	F3 Macroemulsion White/milk		F8 White Clear
	F4 Macroemulsion White/milk		F9 White Clear
	F5 Bluish/cloudy		F10 White Clear

Table 4.8 Nanoemulgel Formulation For 5% of mixed Carbopol 940 appearance

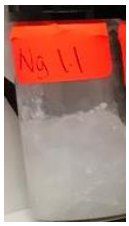
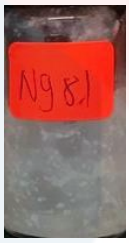
	Ng1.1 White Milk		Ng6.1 White Milk
	Ng2.1 White Milk		Ng7.1 White milk
	Ng3.1 White Milk		Ng8.1 White milk
	Ng4.1 White Milk		Ng9.1 White Milk
	Ng5.1 White Milk		Ng10.1 White Transparent

Table 4.9 Nanoemulgel Formulation For 10% of mixed Carbopol 940 appearance

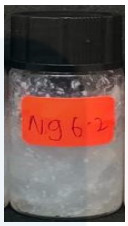
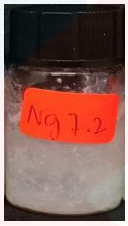
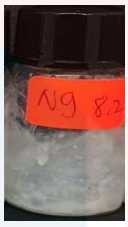
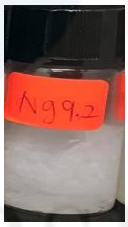
	Ng1.2 White Milk		Ng6.2 White Milk
	Ng2.2 White Milk		Ng7.2 White Milk
	Ng3.2 White Milk		Ng8.2 White Milk
	Ng4.2 White Milk		Ng9.2 White Milk
	Ng5.2 White Milk		Ng10.2 White Transparent

Table 4.10 Nanoemulgel Formulation For 15% of mixed Carbopol 940 appearance

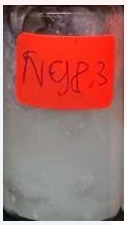
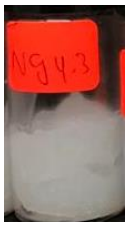
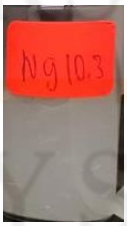
	Ng1.3 White Milk		Ng6.3 White Milk
	Ng2.3 White Milk		Ng7.3 White Milk
	Ng3.3 White Milk		Ng8.3 White Milk
	Ng4.3 White Milk		Ng9.3 White Milk
	Ng5.3 White Milk		Ng10.3 White Milk

Table 4.11 Nanoemulsion from nanoemulgel 5% of mixed of Carbopol 940 appearance

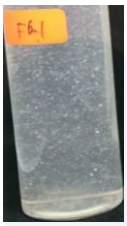
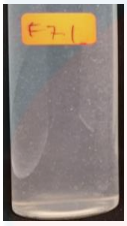
	F1.1 Cloudy Transparent		F6.1 Cloudy Transparent
	F2.1 Cloudy Transparent		F7.1 Cloudy Transparent
	F3.1 Cloudy Transparent		F8.1 Cloudy Transparent
	F4.1 Cloudy Transparent		F9.1 Cloudy Transparent
	F5.1 Cloudy Transparent		F10.1 Cloudy Transparent

Table 4.12 Nanoemulsion from nanoemulgel 10% of mixed of Carbopol 940 appearance

	F1.2 Cloudy Transparent		F6.2 Cloudy Transparent
	F2.2 Cloudy Transparent		F7.2 Cloudy Transparent
	F3.2 Cloudy Transparent		F8.2 Cloudy Transparent
	F4.2 Cloudy Transparent		F9.2 Cloudy Transparent
	F5.2 Cloudy Transparent		F10.2 Cloudy Transparent

Table 4.13 Nanoemulsion from nanoemulgel 15% of mixed of Carbopol 940 appearance

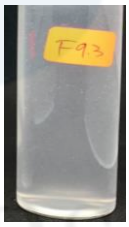
	F1.3 Cloudy Transparent		F6.3 Cloudy Transparent
	F2.3 Cloudy Transparent		F7.3 Cloudy Transparent
	F3.3 Cloudy Transparent		F8.3 Cloudy Transparent
	F4.3 Cloudy Transparent		F9.3 Cloudy Transparent
	F5.3 Cloudy Transparent		F10.3 Cloudy Transparent

Table 4.14 Nanoemulgel from Concentrated F5 (3331) appearance

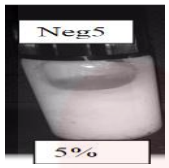
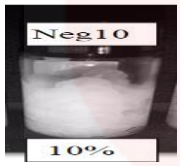
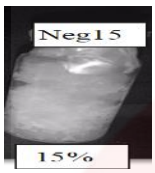
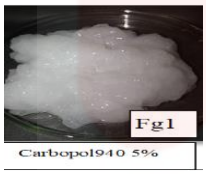
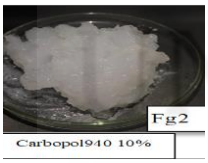
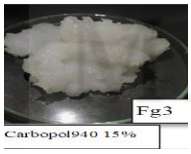
	Neg5 White Milk
	Neg10 White Milk
	Neg15 White Milk

Table 4.15 Nanoemulgel F5 (3331) appearance

	Fg1 White Milk
	Fg2 White Milk
	Fg3 White Milk

The appearance of nanoemulsion formulations, as depicted in Table 4.7, was observed. The color appearance of the nanoemulsion formulations (F1, F2, F5, and F6) presented a bluish and cloudy aspect, likely due to the small droplet size. Conversely, the macroemulsions (F3 and F4) exhibited a white/milky appearance attributed to larger droplet sizes scattering light uniformly. In contrast, the microemulsion formulations (F7, F8, F9, and F10) appeared white clear, indicative of high transparency and stability with droplets dispersed evenly at a size much smaller than those in macroemulsions. These distinct color appearances reflected the different emulsion types and provided valuable insights into their stability and formulation characteristics.

Table 4.8 provided the appearance of Nanoemulgel formulations containing 5% mixed Carbopol 940. The majority of formulations (Ng1.1 to Ng9.1) exhibited a consistent white milk appearance, indicative of a homogeneous dispersion of emulsion droplets within the gel matrix. However, formulation Ng10.1 stood out with a white transparent appearance. In Table 4.9, Nanoemulgel formulations with 10% mixed Carbopol 940 exhibited a consistent white milk appearance for Ng1.2 through Ng9.2, indicating a uniform dispersion of emulsion droplets within the gel matrix across these formulations. However, Ng10.2 stood out with a white transparent appearance, similar to Ng10.1 in the previous table containing 5% mixed Carbopol 940.

Table 4.10 showed Nanoemulgel formulations with 15% mixed Carbopol 940, all of which exhibited a consistent white milk appearance from Ng1.3 to Ng10.3. Table 4.11 presented Nanoemulsion formulations derived from Nanoemulgel containing 5% mixed Carbopol 940, all of which displayed a cloudy transparent appearance. Table 4.12 showed Nanoemulsion formulations obtained from Nanoemulgel with 10% mixed Carbopol 940, all exhibiting a

consistent cloudy transparent appearance. In Table 4.13, Nanoemulsion formulations derived from Nanoemulgel with 15% mixed Carbopol 940 exhibited a consistent cloudy transparent appearance across all formulations, from F1.3 to F10.3. In Table 4.14, Nanoemulgel formulations derived from Concentrated F5 (3331) displayed a consistent white milk appearance across all formulations, including Neg5, Neg10, and Neg15. In Table 4.15, Nanoemulgel formulations of F5 (3331) exhibited a consistent white milk appearance across all formulations, including Fg1, Fg2, and Fg3.

All the solutions were different in appearance from each other; therefore, it was easy to determine the one that was nanoemulsion. These distinct color appearances reflect the different emulsion types and provide valuable insights into their stability and formulation characteristics.

4.2.2 Tyndall Effect

The Tyndall effect test was done on nanoemulsion, macroemulsion, and water to see the differences of appearance between each liquid. The result was as shown in Figure 4.9.

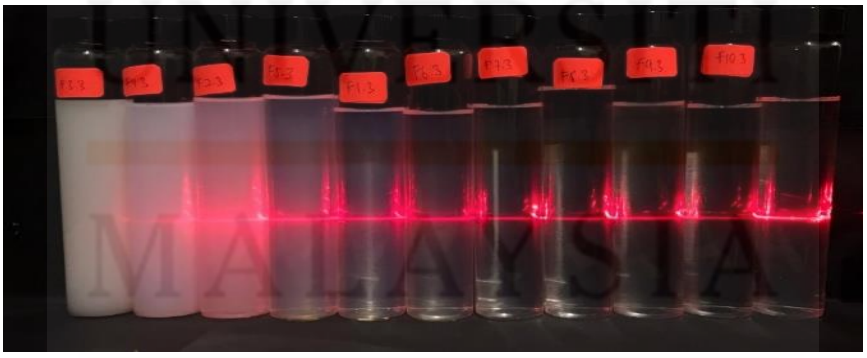


Figure 4.9: The tyndall effect test on macroemulsion, nanoemulsion, and water.

With the exception of bottle F3.3, all of the bottles holding the nanoemulsion—bottles F10.3 to F1.3—were confirmed to have had laser penetration. Bottles F3.3, containing macroemulsion and water, respectively, showed no signs of light beam penetration. This result shows that nanoemulsion was a colloid and water was a true solution. A colloid exhibits a visible beam because of the particles found in an authentic solution. This causes light to be unable to pass through it without dispersing, which explains the visible light on the solution in the container. The amount of scattering however depends on the frequency of the light and density of particles in the solutions as well (Fernandes et al., 2014).

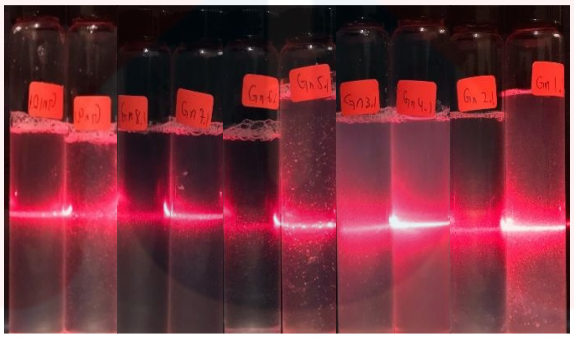


Figure 4.10: The Tyndall effect on nanoemulsion from formulation F5 nanoemulgel containing 5%, 10%, and 15% of agent gel.

The results of the Tyndall effect test on nanoemulsion F1 to F10 are shown in Figure 4.10, overall sample nanoemulsion from formulation F5 nanoemulgel containing 5%, 10%, and 15% of agent gel. It was observed that it illuminated the beam's path, making it visible. This happened as a result of the nanoemulsion's colloidal particle absorbing energy and then distributing it throughout.

4.2.3 Stability Test

The stability test was conducted by observing all the samples of nanoemulsion at room temperature. The test was carried out over a period of 14 days. The objective of the stability test was to determine the duration during which the nanoemulsion lost its stability based on visual observations of each sample.

Figure 4.11: Day 1

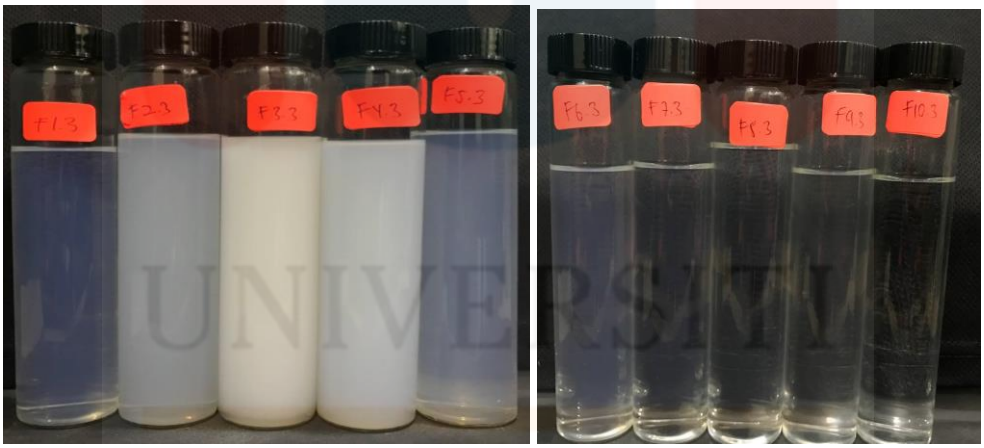


Figure 4.12: Day 14

According to Figure 4.11 observations of each sample, not a single sample separated on the day it was created. After 14 days, the status of every sample is shown in Figure 4.12. Since there is no separation, it may be said that samples F1, F2, F3, F4, F5, F6, F7, F8, F9, and F10 are stable. According to Gupta (2016), nanoemulsions are kinetically stable after some time phase

separation can occur. Samples F1, F2, F3, F4, F5 F6, F7, F8, F9, and F10 remain stable due to their small droplet size which causes them to be kinetically stable over a long time scale so that no separation occurs (Ankur Gupta et al., 2010).

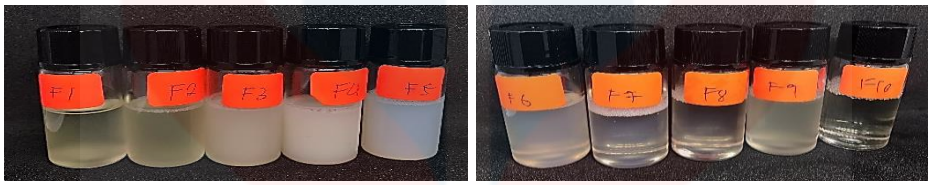


Figure 4.13: Concentrated Nanoemulsion Formulation Day 1

Figure 4.14: Concentrated Nanoemulsion Formulation Day 14

For every sample, none was taken out of the sample on the day it was made, as shown by the observation in Figure 4.13. Fourteen days after, Figure 4.14 displayed the state of half of the samples. As there wasn't any separation, samples F6, F7, F8, F9, and F10 could be deemed stable. That being said, F1, F2, F3, F4, and F5 were unstable because of their isolation.

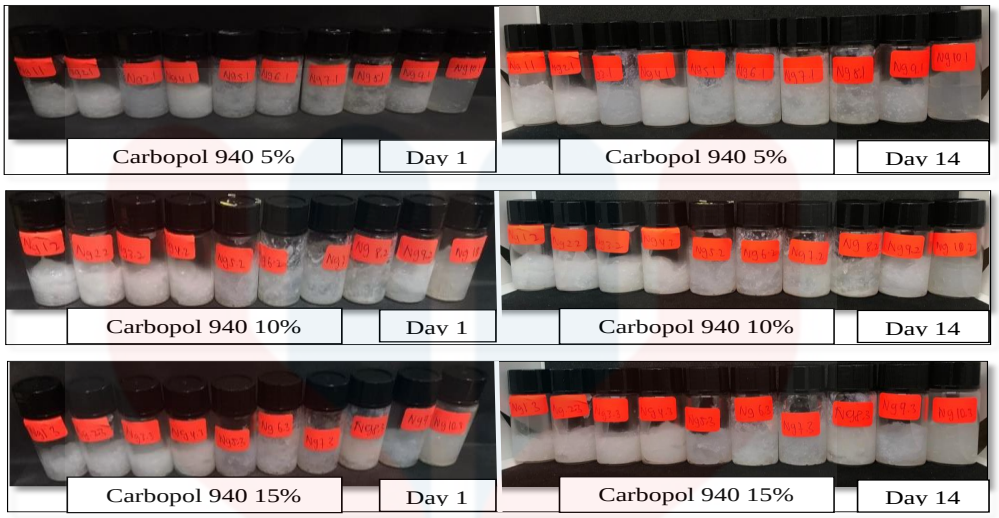


Figure 4.15: Stability Nanoemulgel from day 1 to day 14

Based on the observation of each sample in Figure 4.15, all nanoemulgel samples containing 5%, 10%, and 15% did not separate on the first day they were made. Figure 4.15 also shows the state of all samples after 14 days. It can be concluded that nanoemulgel samples containing 5%, 10%, and 15% are stable because no separation occurs.

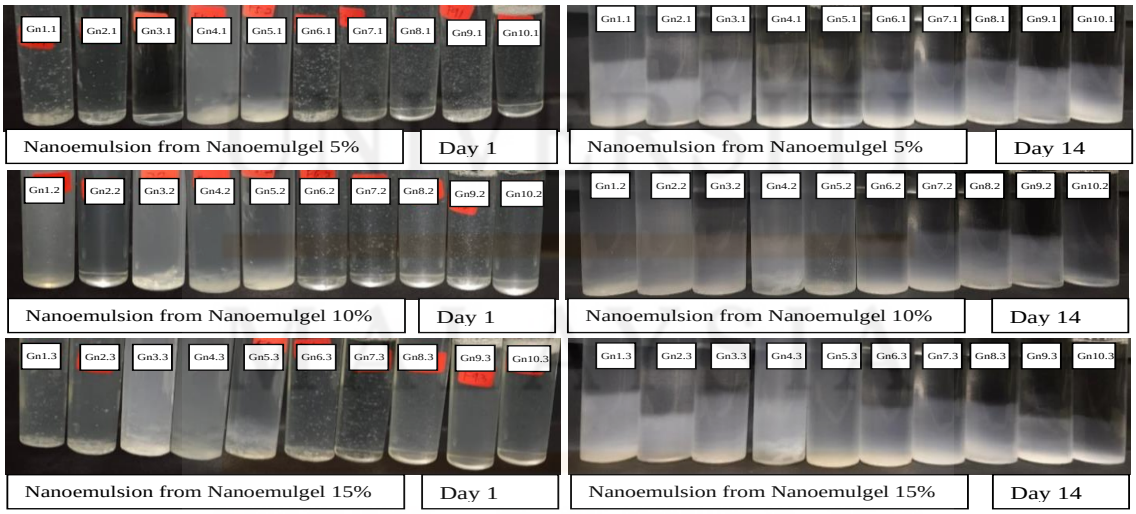


Figure 4.16: Nanoemulsion from Nanoemulgel with 5%, 10% and 15% ceoncentration from day 1 to day 14

The observations of the 14-day samples, which displayed the states of each sample individually, indicated that none of the nanoemulsion samples from the nanoemulgel containing 5%, 10%, and 15% separated on the day they were created. Given that separation happens, it was possible to deduce that the nanoemulsion samples made from nanoemulgel containing 5%, 10%, and 15% were unstable.

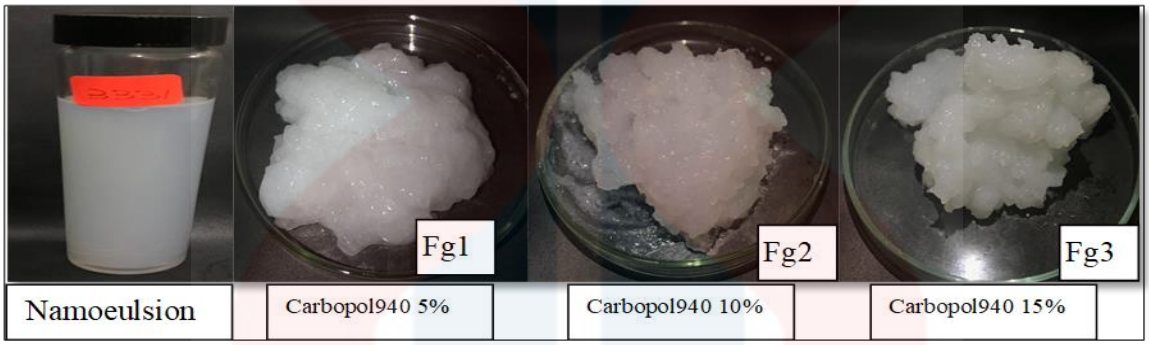


Figure 4.17: Nanoemulgel F5 (3331) day 1

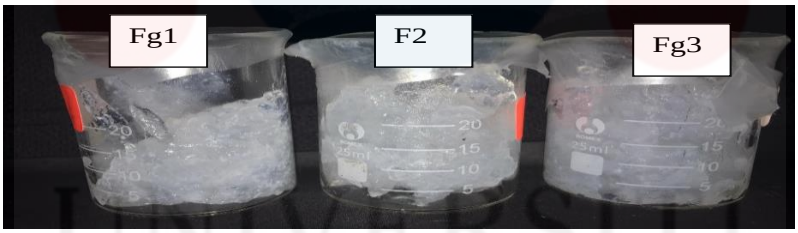


Figure 4.18: Nanoemulgel F5 (3331) day 14

In accordance with the observations of every sample depicted in Figure 4.17, on the first day of their creation, none of the Nanoemulgel F5 (3331) samples separated. After 14 days, Figure 4.18 demonstrated that every sample remained stable. Since segregation did not occur, it can be concluded that the Nanoemulgel F5 (3331) sample was stable.

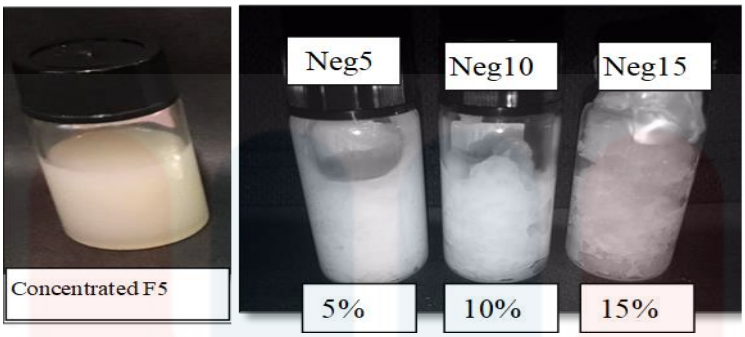


Figure 4.19: Nanoemulgel from Concentrated F5 (3331) day 1

Figure 4.20: Nanoemulgel from Concentrated F5 (3331) day 14

The observations for each sample, as depicted in Figure 4.19, indicated that none of the samples had separated on the day the concentrated F5 (3331) nanoemulgel was produced. Figure 4.20 illustrated that all samples remained stable after 14 days. Consequently, it can be inferred that the sample, nanoemulgel from Concentrated F5 (3331), was stable as no separation occurred.

Inconclusion, the stability test results show promising outcomes, with the nanoemulsion and nanoemulgel samples remaining stable over a 14-day period. This stability is attributed to the small droplet size of the nanoemulsion, contributing to its kinetically stable nature.

4.2.4 PH Measurument

To demonstrate the pH-responsive behavior of the nanoemulsion, the interfacial tension between water and oil at different pH values was monitored at room temperature (Ren et al., 2021). Skin pH is normally acidic, ranging between 4 and 6, while the body's internal environment maintains a neutral to slightly alkaline pH (~7.4) (Prakash et al., 2017).

Table 4.16 pH reading of samples Nanoemulsion.

Sampel	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
pH measurement	5.7	6.1	6.2	6.3	6.4	6.4	6.5	6.5	6.3	6.5

Table 4.17 pH reading of samples concentrated Nanoemulsion.

Sampel	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
pHmeasurement	6.5	6.7	6.6	6.5	6.5	6.4	6.5	6.8	6.0	6.1

Nanoemulsion formulations F1 through F10 show a stable pH range of 5.7 to 6.5 in Table 4.7. This pH level's constancy is admirable and consistent with the natural acidity of the skin, suggesting excellent skin compatibility. The degree of acidity (pH) is a very important parameter in a cosmetic product because the pH of cosmetics influences its absorption on the skin (Indriati et al., 2018).

Table 4.18 Ph reading on Nanoemulsion sample from Nanoemulgel Formulation 5%, 10% and 15%.

Sample Nanoemulsion (Gn) / Percent of Nanoemulgel and Carbopol 940 mixed (%)	pH measurement									
	Gn1	Gn2	Gn3	Gn4	Gn5	Gn6	Gn7	Gn8	Gn9	Gn10
5	5.6	5.5	5.4	5.5	5.5	5.6	5.6	5.9	5.9	6.0
10	6.2	6.3	6.6	6.5	6.5	6.7	6.4	6.4	6.4	6.4
15	6.3	6.3	6.4	6.4	6.2	6.3	6.3	6.3	6.3	6.5

Table 4.19 The average pH reading of Nanoemulsion sample from Nanoemulgel Formulation 5%, 10% and 15%.

Samples	pH Measurement
Gn 5%	5.61 ± 0.2606
Gn10%	6.54±0.181
Gn15%	6.35±0.1389

Values are expressed as mean ± SD (n=10).

Table 4.20 The average pH reading of Nanoemulgel Formulation 5%, 10% and 15%.

Sample Nanoemulgel (Ng) / Percent of Nanoemulgel and Carbopol 940 mixed (%)	pH measurement									
	Ng1	Ng2	Ng3	Ng4	Ng5	Ng6	Ng7	Ng8	Ng9	Ng10
5	3.5	3.5	3.4	3.4	3.3	3.4	3.8	3.7	3.7	3.7
10	3.9	3.7	3.6	3.3	3.7	3.7	3.8	3.9	3.8	3.2
15	3.6	3.4	3.4	3.6	2.9	3.4	3.4	3.4	3.2	3.2

Values are expressed as mean ± SD (n=10).

Table 4.21 Ph reading test on Nanoemulgel Formulation 5%, 10% and 15%.

Samples	pH Measurement
Gn 5%	3.54±0.1651
Gn10%	3.74±0.3521
Gn15%	3.43±0.1715

Values are expressed as mean ± SD (n=10).

Table 4.22 Ph reading nanoemulgel from concentrated nanoemulsion Formulation 5%, 10% and 15%.

Sampel	5%	10%	15%
pH measurement	3.7	3.5	3.0

The pH measurements provided for samples at concentrations of 5%, 10%, and 15% represented the acidity or alkalinity levels of each respective solution. The pH measurements of 3.7, 3.5, and 3.0 indicated that the samples were all acidic, with a decreasing trend in acidity as the concentration increased.

Table 4.23 Ph reading nanoemulgel from nanoemulsion Formulation F1.

Sampel	Neg5	Neg10	Neg15
pH measurement	2.9	2.9	3.2

The pH measurement provided for the sample indicated acidity or alkalinity levels. A pH value of 2.9 suggested a highly acidic environment, and this acidity remained consistent across the three samples with values of 2.9, 2.9, and 3.2 for Neg5, Neg10, and Neg15, respectively. The pH scale ranges from 0 to 14, where values below 7 indicate acidity, 7 is neutral, and values

above 7 signify alkalinity. In this case, the sample exhibited a consistently low pH, signifying a strongly acidic nature. The slight increase from 2.9 to 3.2 may have indicated a marginal decrease in acidity, but overall, the samples remained highly acidic.

Overall, the pH measurements provide insights into the acidity levels of the formulations. The results demonstrate that the pH values are within a desirable range for skin compatibility, emphasizing the potential use of these formulations in cosmetic or dermatological applications

4.2.5 Viscosity Test

A maximum of 100 mL of gel was put into a container, and then placed on a viscometer with spindle no. 64 installed. Then, the spindle was lowered onto the gel to the specified limit. Next, we set the speed to 0.6 rpm and used the viscosity value shown on the tool (Nurman et al., 2019).

Figure 4.21: Measurement Viscosity of nanoemulsion sample from nanoemulgel 5%, 10% and 15% of Carbopol 940.

Nanoemulsion samples from nanoemulgel formulation with 5%. 10% and 15% of Carbopol 940. Formulation at concentrations of 5%, 10% and 15% may have a viscosity that is

too low to be measured accurately by the viscometer, therefore all the samples get L unit which means the viscosity value is below the measuring range. Instruments may not be sensitive enough to detect these lower viscosity values.

Table 4.24 Averege viscosity of Nanoemulgel from concentrated nanoemulsion formulation.

Sample Nanoemulgel (Ng) / Percent of Nanoemulgel and Carbopol 940 mixed (%)	Viscometer (mPa.s)									
	Ng1	Ng2	Ng3	Ng4	Ng5	Ng6	Ng7	Ng8	Ng9	Ng 10
5	1.05	1.05	1.5	1.05	1.06	1.07	1.07	1.09	1.09	1.09
10	2.03	2.03	2.03	2.07	2.07	2.07	2.08	2.09	2.09	2.09
15	3.10	3.10	3.12	3.14	3.14	3.16	3.16	3.16	3.18	3.18

Table 4.25 Viscosity of Nanoemulgel from Concentrated F5 (3331)

Sample / Unit	5%	10%	15%
mPa.s	3.0	3.5	3.7

Table 4.26 Viscosity of Nanoemulgel from Nanoemulsion F5 (3331)

Sample / Unit	Neg1 5%	Neg2 10%	Neg3 15%
mPa.s	3.64	4.02	5.06

The resulting nanoemulgels exhibited a milky white and homogeneous appearance, and their viscosity increased proportionally with higher concentrations of Carbopol 940. The

formulations demonstrated excellent stability over a two-week observation period at room temperature, with no observed phase separation, change in consistency, or color. The viscosity measurements, as detailed in Tables 4.15, highlighted a clear trend: nanoemulgels with higher Carbopol 940 concentrations resulted in thicker and more viscous formulations. For instance, the 15% nanoemulgel displayed a significantly higher viscosity range (3.10 mPa.s to 3.18 mPa.s) compared to the 5% and 10% nanoemulgels, indicating the direct impact of Carbopol 940 concentration on the rheological properties of the nanoemulgel. Similarly for Table 4.16 viscosity of 15% nanoemulgel shows a much higher viscosity range of 3.7 mPa.s, than compared to nanoemulgel 5% and 10%, (3.0 mPa.s and 3.5 mPa.s).

Furthermore, a detailed comparison of viscosity measurements for different concentrations and formulations, particularly within Table 4.17 for nanoemulsion formulation F5 (3331), provided insights into the nuanced variations. Notably, the viscosity measurements for Neg1 and Neg2 were 3.64 mPa.s and 4.02 mPa.s, respectively, while Neg3 exhibited a higher viscosity of 5.06 mPa.s. This direct comparison allowed researchers and formulators to understand the relative thickness of each nanoemulgel formulation and tailor their selection based on specific application requirements.

The role of quality control in ensuring optimal viscosity. Manufacturers rely on quality control measures to ensure that their products meet performance, safety, and regulatory standards (Lai, 2005). Also Proper quality control procedures can catch issues, such as inconsistencies in viscosity or other properties before the detergent reaches consumers. Liquid detergent viscosity is a key factor in the overall performance and consumer appeal of detergent products. By

understanding and controlling detergent viscosity, manufacturers can develop products that cater to consumer preferences while maintaining cleaning effectiveness (Lai, 2005).

The incorporation of Carbopol 940 in the formulation of nanoemulgels established a clear relationship between the concentration of the thickening agent and the resulting viscosity. The provided detailed viscosity measurements in Tables 4.15, 4.16, and 4.17 underscored this correlation, highlighting the direct impact of Carbopol 940 concentration on the rheological properties of the nanoemulgels. Notably, as observed in Table 4.15, the 15% nanoemulgel consistently exhibited a significantly higher viscosity range compared to its 5% and 10% counterparts, emphasizing the proportional increase in viscosity with higher concentrations of Carbopol 940. The nuanced variations in viscosity measurements, particularly detailed in Table 4.17 for nanoemulsion formulation F5 (3331), further elucidated the tailored control that formulators could exercise. The direct comparison of viscosity measurements enabled researchers to comprehend the relative thickness of each nanoemulgel formulation. This insight facilitated the customization of formulations based on specific application requirements, such as stability, consistency, and the intended method of application. In conclusion the optimal viscosity depends on the specific application and intended use of the product. There is no one-size-fits-all answer, as different products and processes require different viscosity levels for optimal performance. In some cases, a lower viscosity may be desirable for easy spreading or application, while in others, a higher viscosity may be needed for better stability or adherence to surfaces. Different applications have unique requirements that dictate the ideal viscosity of a formulation.

4.2.6 Spreadibility Test

The effective spreadability of nanoemulgel is a vital criterion in choosing a topical delivery system. The spreadability of various nanoemulgel formulations was assessed and recorded in Table, with the obtained values deemed satisfactory and meeting the established standards. This adherence to the standard range is crucial for ensuring the uniform and efficient application of the formulation on the skin, enhancing its potential for successful drug delivery and therapeutic effectiveness. Larger value shows better spreadability that indicates the contentment of the formulation when applied to the skin, spreads easily, and displays the maximum slip and drag (Zaudin et al., 2022). From the result, Neg10 recorded the largest value of spreadability.

Table 4.27 Average diameter spreadability of nanoemulgel

Sample Nanoemulgel (Ng) / Percent of Nanoemulgel and Carbopol 940 mixed (%)	Spreadability (cm)									
	Ng1	Ng2	Ng3	Ng4	Ng5	Ng6	Ng7	Ng8	Ng9	Ng 10
5	2.2	1.9	1.5	2.5	1.6	2.2	2.2	2.0	1.5	1.5
10	1.8	1.9	1.8	1.7	1.6	1.6	2.0	2.2	2.0	1.8
15	1.5	1.7	1.7	1.9	1.6	1.7	1.6	1.7	1.6	1.6

Table 4.28 Spreadability of concentrated nanoemulgel F1

Sample Concentrated Nanoemulgel F1 / Percent of Nanoemulgel and Carbopol 940 mixed (%)	Spreadability (cm)		
5	2.0	1.9	2.0
10	2.1	2.0	1.9
15	1.5	1.5	1.4

Table 4.29 Spreadability of Nanoemulgel Formulation F1

Sample Concentrated Nanoemulgel F1 / Percent of Nanoemulgel and Carbopol 940 mixed (%)	Spreadability (cm)		
5	2.0	1.9	2.0
10	2.1	2.0	1.9
15	1.5	1.5	1.4

Table 4.30 Spreadability of nanoemulgel

Formulation	Spreadibility (cm)
Ng 5%	1.97 ± 0.336
Ng 10%	1.84 ± 0.04
Ng 15%	1.67 ± 0.08

*Values are expressed as mean ± SD (n=10)

Table 4.21 presented the spreadability of nanoemulgel formulations at different concentrations, denoted as Ng 5%, Ng 10%, and Ng 15%. The spreadability values, expressed in

centimeters, were measured and reported as mean ± standard deviation (SD) based on 10 observations. The results revealed a decreasing trend in spreadability with increasing nanoemulgel concentration. Specifically, Ng 5% exhibited the highest spreadability at 1.97 ± 0.336 cm, followed by Ng 10% with a slightly reduced spreadability of 1.84 ± 0.04 cm. The lowest spreadability was observed for Ng 15%, recording 1.67 ± 0.08 cm. This data suggested that the formulation with 5% nanoemulsion content provided the most favorable spreadability among the tested concentrations.

Table 4.31 Spreadability of Nanoemulgel from concentrated nanoemulsion F1

Sampel	Spreadibility (cm)
5%	1.97 ± 0.0423
10%	1.67 ± 0.3421
15%	1.43 ± 0.0471

*Values are expressed as mean ± SD (n=3)

Table 4.22 illustrated the spreadability of Nanoemulgel from concentrated nanoemulsion F1 at different concentrations (5%, 10%, and 15%). As the concentration increased, spreadability decreased, with values of 1.97 ± 0.0423 cm, 1.67 ± 0.3421 cm, and 1.43 ± 0.0471 cm for 5%, 10%, and 15%, respectively. This suggested that higher nanoemulsion concentrations resulted in less spreadable nanoemulgels, emphasizing the need to consider concentration effects during formulation for optimal application and user experience.

Table 4.32 Spreadability nanoemulgel F1

Sampel	Spreadibility (cm)
Neg5%	1.97±0.0379
Neg10%	2.0±0.0820
Neg15%	1.47±0.0300

*Values are expressed as mean ± SD (n=3)

Table 4.23 compared the spreadability of nanoemulgel formulation F1 at different concentrations (Neg5%, Neg10%, Neg15%). The results showed that F1 at Neg10% exhibited the highest spreadability (2.0±0.0820 cm), surpassing Neg5% (1.97±0.0379 cm) and Neg15% (1.47±0.0300 cm). This suggested that a 10% concentration was optimal for achieving effective coverage and application of the nanoemulgel, highlighting its superior spreadability compared to other concentrations.

In conclusion, the data presented in the spreadability tests indicate that the concentration of nanoemulsion in the nanoemulgel formulation significantly influences the spreadability of the final product. The findings highlight the importance of considering the desired application and user experience when selecting the concentration of nanoemulsion and nanoemulgel in the formulation.

CHAPTER 5

CONCLUSION AND RECOMMENDATION

5.1 Conclusion

The main objective is to investigate the formulation and long-term stability of nanoemulsions, in addition to their incorporation into gels suitable for topical use. During the process of formulation, soybean oil, surfactant, and co-surfactant were included in accordance with the stated ratios provided in Wang's (2009) instructions. Stable nanoemulsions were successfully generated at the designated sites on the ternary phase diagram, demonstrating success. This outcome is anticipated, considering the techniques used in the creation of nanoemulsions. Incorporating Carbopol 940, a topical polymer, with nanoemulsions enables the production of nanoemulgels. The results demonstrate the presence of stable nanoemulgels across different concentrations of Carbopol 940. The protocol for combining nanoemulsion with Carbopol 940 at concentrations of 5%, 10%, and 15% is well explained in tables and figures.

The research investigates the rheology of nanoemulgels by analysing their viscosity and spreadability, both of which play a crucial role in topical formulations. The stability of both nanoemulsions and nanoemulgels, including concentrated forms, remained unchanged for a period of 14 days. This corresponds to the kinetic stability of nanoemulsions. Furthermore, the pH measurements fall within the range that is gentle on the skin, guaranteeing that the formulations of the products retain a skin-friendly atmosphere. These results indicate that the synthesised nanoemulsions and nanoemulgels are appropriate for use on the skin's surface.

The study follows nanoemulsion production standards and earlier research by using a ternary phase diagram and certain surfactant and co-surfactant ratios. The research agrees that nanoemulsions are stable throughout time, which is significant for their application in various formulations. This study's innovation is adding Carbopol 940 to nanoemulsions to make nanoemulgels. Although there aren't many similarities with the literature in this situation, the study provides the framework for additional gelling agent and nanoemulsion blending research. The observed viscosity trends, where Carbopol 940 concentration increases viscosity, follow rheological principles that control gel compositions. The duration of the stability testing is another drawback. The 14-day timeframe may not have caught any long-term stability problems that could have developed over time. Even if the findings show stability during the measured timescale, longer stability tests are necessary for a more thorough analysis of the prepared nanoemulsions and nanoemulgels.

In conclusion, through the development of stable nanoemulsions and nanoemulgels suitable for potential topical applications, the study effectively addresses the research objective. The analysis of the data suggests that stable nanoemulsions were successfully produced at the

selected formulation locations on the ternary phase diagram. The addition of Carbopol 940 thereafter produced nanoemulgels in different amounts. The formulations' potential for topical use is supported by stability testing, pH readings, and rheological analyses taken as a whole. Comparisons with existing literature verify the study's nanoemulsion creation technique, which also forms the foundation for the novel aspect of introducing nanoemulsions into gels. It is acknowledged that there are a number of limitations, including the components' specificity and the short stability testing period. These constraints guide the cautious interpretation and application of the results in broader contexts.

5.2 RECOMMENDATION

In order to further the field's knowledge of nanoemulsions and nanoemulgels, it is advised to expand the range of specialised testing. Dynamic Light Scattering (DLS) analysis may be included to get important insights into the dynamics of size distribution stability over time. Furthermore, by providing information on viscoelastic characteristics, rheological experiments using a rheometer may direct the creation of goods with desired texture and application qualities. Zeta potential measurements play a critical role in forecasting the stability of colloidal systems, and high-resolution pictures obtained using Transmission Electron Microscopy (TEM) may shed light on nanoscale structures. Analysis using Fourier-Transform Infrared Spectroscopy (FTIR) may uncover molecular interactions and provide insight into how well formulation components work together. It is also advised to do thorough analyses using accelerated stability tests, skin penetration studies, cytotoxicity assessments, and environmental impact analysis to determine shelf life, bioavailability, safety, and sustainability.. A nanoemulgel

formulation with 5% Carbopol 940 is recommended for optimal results, as higher concentrations of 10% and 15% have been observed to result in excessive thickness and difficulty in achieving a suitable gel consistency. The 5% concentration strikes a balance, providing the desired gel formulation without being excessively thick. Moreover, lower concentrations may help prevent the formation of gel blobs over time. This optimal formulation ensures a stable and effective nanoemulgel with improved consistency for practical application. At the same time, it is recommended to increase the number of points on the ternary phase diagram in order to facilitate the methodical creation of a wider range of nanoemulsion formulations. This comprehensive approach guarantees a deep understanding of nanoemulsions and nanoemulgels, opening the door to their ideal formulation and a wide range of uses

REFERENCES

Aithal, G. C., Narayan, R., & Nayak, U. Y. (2020). Nanoemulgel: A Promising Phase in Drug Delivery. *Current Pharmaceutical Design*, *26*(2), 279–291. https://doi.org/10.2174/1381612826666191226100241

Chuo, S. C., & Mohd Setapar, S. H. (2022, January 1). 15 - Application of nanoemulsion in cosmetics (S. H. Mohd Setapar, A. Ahmad, & M. Jawaid, Eds.). Retrieved from ScienceDirectwebsite:https://www.sciencedirect.com/science/article/abs/pii/B9780128229675000011#

Gurpreet, K., & Singh, S. K. (2018). Review of Nanoemulsion Formulation and Characterization Techniques. *Indian Journal of Pharmaceutical Sciences*, *80*(5), 781–789. https://doi.org/10.4172/pharmaceutical-sciences.1000422

Hartmann, T. (2023, January 10). Nanoemulgel: A Novel Nano Carrier as a Tool for Topical Drug Delivery. Retrieved May 16, 2023, from Pharma Excipients website: https://www.pharmaexcipients.com/news/nanoemulgel-topical-drug-delivery/

Mason, T. G., Wilking, J., K. Meleson, Chang, C. B., & Graves, S. (2017). Nanoemulsions: formation, structure, and physical properties. Retrieved May 17, 2023, from Journal of Physics:CondensedMatterwebsite:https://www.semanticscholar.org/paper/Nanoemulsions%3A-formation%2Cstructure%2C-and-physical-Mason Wilking/99ebea3d10d7a15f60437a38826c0f5ef94ba317

Ting, T. C., Amat Rahim, N. F., Che Zaudin, N. A., Abdullah, N. H., Mohamad, M., Shoparwe, N. F., Mhd Ramle, S. F., Aimi, Z., Abdul Hamid, Z. A., & Yusof, A. H. (2020). Development and Characterization of Nanoemulgel Containing *Piper betle* Essential Oil as Active Ingredient. Retrieved from IOP Conference Series: Earth and Environmental Science website: https://www.semanticscholar.org/paper/Development-and-Characterization-of-

Mahipal Reddy Donthi, Siva Mala Munnangi, Kowthavarapu Venkata Krishna, Ranendra Narayan Saha, Gautam Singhvi, & Sunil Kumar Dubey. (2023). Nanoemulgel: A Novel Nano Carrier as a Tool for Topical Drug Delivery. Pharmaceutics, 15(1), 164–164. https://doi.org/10.3390/pharmaceutics15010164

Khare, A., Ansari, A., Patki, P., & Perampalli, N. (2021). DESIGN AND DEVELOPMENT OF NANOEMULSION FORMULATION: A REVIEW. DESIGN and DEVELOPMENT of NANOEMULSION FORMULATION: A REVIEW, 9(7), 2320–2882. Retrieved from https://ijcrt.org/papers/IJCRT2107133.pdf

Ashaolu, T. J. (2021). Nanoemulsions for health, food, and cosmetics: a review. Environmental Chemistry Letters. https://doi.org/10.1007/s10311-021-01216-9

S. Mohapatra, S., Ranjan, S., Dasgupta, N., Kumar Mishra, R., & Thomas, S. (2019). Applications of Targeted Nano Drugs and Delivery Systems. Elsevier. https://doi.org/10.1016/c2017-0-00274-4

Chime, S. A., Kenechukwu, F. C., & Attama, A. A. (2014). Nanoemulsions — Advances in Formulation, Characterization and Applications in Drug Delivery. In www.intechopen.com. IntechOpen. Retrieved from https://www.intechopen.com/chapters/47116

Azeez, A. R., & Alkotaji, M. (2021). NANOEMULGEL AS A RECENT DRUG DELIVERY SYSTEM. Military Medical Science Letters. https://doi.org/10.31482/mmsl.2021.035

Patra, J. K., Das, G., Fraceto, L. F., Campos, E. V. R., Rodriguez-Torres, M. del P., Acosta-Torres, L. S., … Shin, H.-S. (2018). Nano based drug delivery systems: recent developments and future prospects. Journal of Nanobiotechnology, 16(1). https://doi.org/10.1186/s12951-018-0392-8

Omlor, A. J., Nguyen, J., Bals, R., & Dinh, Q. T. (2015). Nanotechnology in respiratory medicine. Respiratory Research, 16(1). https://doi.org/10.1186/s12931-015-0223-5

Ren, G., Li, B., Ren, L., Lu, D., Zhang, P., Tian, L., … Sun, D. (2021). pH-Responsive Nanoemulsions Based on a Dynamic Covalent Surfactant. Nanomaterials, 11(6), 1390. https://doi.org/10.3390/nano11061390

Anand, K., Ray, S., Rahman, M., Shaharyar, A., Bhowmik, R., Bera, R., & Karmakar, S. (2019). Nano-emulgel: Emerging as a Smarter Topical Lipidic Emulsion-based Nanocarrier for Skin Healthcare Applications. Recent Patents on Anti-Infective Drug Discovery, 14(1), 16–35. https://doi.org/10.2174/1574891x14666190717111531

A&D COMPANY, LIMITED (Tokyo, JAPAN). (2009, June). SV Series Sine-wave Vibro Viscometers | Viscometer | Test & Measurement | Products | A&D. Www.aandd.jp. https://www.aandd.jp/products/test_measuring/sv10/sv.html#videos

Indriati, D., Wiendarlina, I. Y., & Carolina, A. S. (2018). Formulation and Evaluation of Anti-Acne Lotion Containing Red Ginger (Zingiber officinalle Roscoe) Essential Oil. Pharmacology and Clinical Pharmacy Research, 3(3), 57–61. https://doi.org/10.15416/pcpr.v3i3.19841

Helmenstine, A. (2022, July 30). Tyndall Effect Definition and Examples. Science Notes and Projects. https://sciencenotes.org/tyndall-effect-definition-and-examples/

Mulia, K., Ramadhan, R. M. A., & Krisanti, E. A. (2018). Formulation and characterization of nanoemulgel mangosteen extract in virgin coconut oil for topical formulation. MATEC Web of Conferences, 156, 01013. https://doi.org/10.1051/matecconf/201815601013

Prakash, C., Bhargava, P., Tiwari, S., Majumdar, B., & Bhargava, R. K. (2017). Skin Surface pH in Acne Vulgaris: Insights from an Observational Study and Review of the Literature. The Journal of Clinical and Aesthetic Dermatology, 10(7), 33–39. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5605222/#B10

Ren, G., Li, B., Ren, L., Lu, D., Zhang, P., Tian, L., Di, W., Shao, W., He, J., & Sun, D. (2021). pH-Responsive Nanoemulsions Based on a Dynamic Covalent Surfactant. Nanomaterials, 11(6), 1390. https://doi.org/10.3390/nano11061390

Sabale, V., Sabale, P., & Kunjwani, H. (2011). Formulation and in vitro evaluation of the topical antiageing preparation of the fruit of Benincasa hispida. Journal of Ayurveda and Integrative Medicine, 2(3), 124. https://doi.org/10.4103/0975-9476.85550

Zaudin, N. A. C., Sulaiman, N. S., Ting, T. C., Ramle, S. F. M., Abdullah, N. H., & Geng, B. J. (2022). Development and characterization of nanoemulsion containing essential oil of Piper betle as the active ingredient via low energy emulsification method. NASA ADS, 2454, 060051. https://doi.org/10.1063/5.0078522

Nurman, S., Yulia, R., Irmayanti, Noor, E., & Candra Sunarti, T. (2019). The Optimization of Gel Preparations Using the Active Compounds of Arabica Coffee Ground Nanoparticles. Scientia Pharmaceutica, 87(4), 32. https://doi.org/10.3390/scipharm87040032

Lai, K.-Y. (2005). Liquid Detergents 2nd Edition. Liquid Detergents, 129, 712. https://doi.org/10.1201/9781420027907

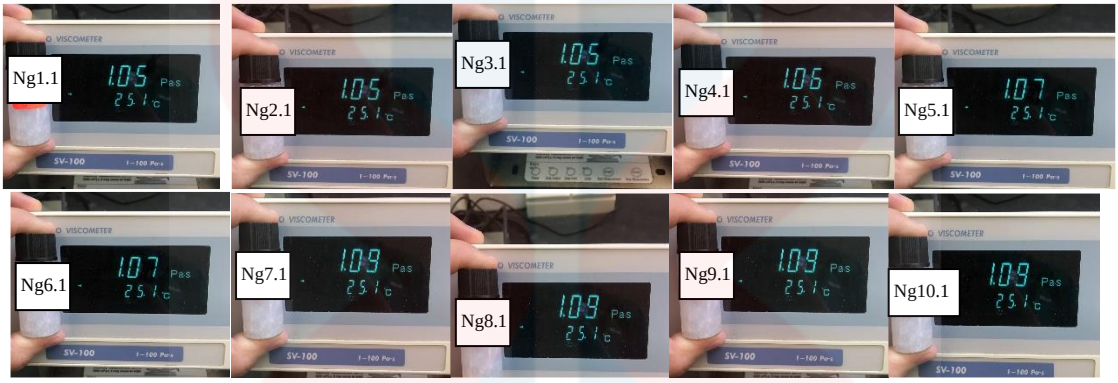
Kulinowski, K., & Lippy, B. (2011). Training Workers on Risks of Nanotechnology. https://tools.niehs.nih.gov/wetp/public/hasl_get_blob.cfm?ID=9094

Bhushan, B. (2017). Introduction to Nanotechnology. Springer Handbook of Nanotechnology, 1–19. https://doi.org/10.1007/978-3-662-54357-3_1

APPENDIX

APPENDIX A

Viscosity Test



Measurement Viscosity of nanoemulsion sample from nanoemulgel 5% of Carbopol 940.

Measurement Viscosity of nanoemulsion sample from nanoemulgel 10% of Carbopol 940.

Measurement Viscosity of nanoemulsion sample from nanoemulgel 15% of Carbopol 940.

Measurement Viscosity of nanoemulgel 5%, 10% and 15% from ceoncentrated nanoemulsion formulation F5

APPENDIX B

PH Measurument

Ph reading test on Nanoemulsion sample from Nanoemulgel Formulation 5%, 10% and 15%.

pH reading of samples Nanoemulsion.

pH reading of samples concentrated Nanoemulsion.