Research Article

Stability Studies of Nano-Scaled Emulsions Containing Ibuprofen for Topical Delivery

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Abstract

Biphasic systems, like emulsions and nano-scaled emulsions, are naturally unstable. The extent and rate of the destabilization process differ from system to another. The stability of such systems upon storage is an important aspect to ensure their abilities to exert the expected effects and consequently render them pharmaceutically acceptable. In the present study, the stability of the nano-scaled emulsion containing newly synthesized palm oil esters (POEs) was assessed under different storage conditions and over specified durations. Three nano-scaled emulsion formulae were chosen for this investigation. They basically comprised ibuprofen as the active ingredient, triethanolamine aqueous solution pH 7.4 as the external phase, POEs as the oil phase, Tween 80 as an emulsifier, Carbopol® 940 as the rheology modifier and menthol or limonene as penetration promoters. The evaluation processes were carried out at several temperatures (4, 25 and 40 °C) with factors, such as droplets size, electrical conductivity, drug content, pH and flow properties were relatively held constant. The data collectively showed that all formulations were stable over an observation period of three months.

Keywords: Ibuprofen, nano-scaled emulsion, palm oil esters, stability

Introduction

Stability studies are most commonly conducted by formulators to provide proofs that their products are acceptable pharmaceutically. The quality of drug products may vary over time under the influence of some environmental factors like temperature, humidity and light, factors which finally set the shelf-life of a pharmaceutical product. Accordingly, several tests have been developed to assess the quality of these products and ensure their content uniformity. Second law of thermodynamics states that biphasic systems, like emulsions, are inherently unstable and the extent and rate of destabilization differ from system to system. Creaming, flocculation [1], coalescence [2], Ostwald ripening [3] and phase inversion [4] are the common mechanisms of emulsion destabilization.

In general, these destabilization mechanism are divided into reversible and irreversible ones. Creaming, the separation of emulsion phases due to the difference in the densities of the dispersed and dispersion phases, is a reversible process. According to Stock's Law of sedimentation, prevention of this process can be achieved by using dispersed phase and dispersion medium of fairly equal densities, decreasing the emulsion globules size and increasing the viscosity of the external phase. [5, 6]

Flocculation is another reversible destabilization process that represents the association of the dispersed droplets via certain weak bonds. This mechanism may lead, in some circumstances, to irreversible coalescence. In systems stabilized by non-ionic surfactants, van der Waals forces are responsible for attracting the dispersed droplets to each other, but they are prevented from being coalesced by repulsion due to steric hindrance. [7] The strength of these van der Walls attractive forces depends, to a large extent, on the radii of the dispersed phase droplets. Decreasing droplets radius usually causes the potential of these attractive forces to decrease. [8] While, increasing the concentration of surfactants in these systems normally leads to a rise in the thickness of their films surrounding the dispersed droplets, which in turn enhances the steric repulsion rendering such emulsions to be more stable. Thus, flocculation, as a mechanism of emulsions destabilization, may not be an important parameter to be evaluated, especially in case of micro- and nano-emulsions as their droplets size is very small and the concentration of surfactant is high.

By contrast, Ostwald ripening and coalescence represent the irreversible mechanisms of emulsions deterioration. Ostwald ripening is the enlargement of a single emulsion droplet due to the variation in chemical potential of the substance contained by the droplets; whereas, coalescence refers to the grouping of two droplets to form a larger one. Ostwald ripening and/or coalescence phenomena lead finally to the separation of these systems into three phases, namely: the internal, external and emulsifier phases. Ostwald ripening is highly correlated with systems that show a wide range of droplets size distribution; therefore, this mechanism is considered as the major stability issue that needs to be addressed by formulators to produce successful micro- or nano-emulsion systems.

Finally, phase inversion is either an attractive or disagreeable phenomenon that mainly depends on its final application. For example, butter making process is an instance on the desirable phase inversion compared to the unwanted cream maturation. [4] In pharmaceutical emulsions, the conversion of the internal phase to the external phase and vise versa is unacceptable and should be extremely avoided.

Emulsified systems stability can be efficiently evaluated under normal storage conditions, i.e. normal temperature, humidity, etc. However, longer period of observation is required, which is in many cases believed to be an obstacle. Therefore, accelerated stability studies using stressed conditions can be carried out to generate stability data quickly and reliably.

Chemically, a degradation or ionization of one or more of the ingredients in the formula can be reflected by a change in formulation pH value. Additionally, incompatibility or degradation of any of the ingredients contained by an emulsion is revealed by their chemical transformation which consequently can produce chemically toxic effect upon usage. Conductivity is a technique commonly used to determine emulsions type whether it is o/w or w/o, in which an aqueous external phase results in a conductive system. The loss of initial system conductivity reveals phase inversion; besides, the measurement of emulsions conductivity at different parts of their containers could be an advanced detection of creaming or sedimentation. [9]

Droplets size measurement of nano-scaled emulsions is a very important factor in evaluating their stability, since a dramatic change in droplets size with time is directly related to internal phase droplets aggregation or association to form larger droplets. [9] Viscosity of the system is an important parameter involved in the formation and continuation of stable emulsions. Relatively, reduction of the viscosity with time can identify a

kinetically unstable emulsion where the free moveable droplets collide with each other and tend to coalesce. Hence, the detection of any change in systems viscosities with time can provide data about their stability.

Overall, dispersed systems should preserve the same number and size of the dispersed droplets in the dispersion media. In other words, the stability of an emulsion is concerned with the continuation of a consistent dispersion of the internal phase in the external phase without showing effective changes in both of them.

In the present study, the stability of selected nano-scaled emulsions was evaluated over reasonable storage duration. Several measures contributing to the stability of nano-scaled emulsions were appraised. The evaluation processes were carried out at several temperatures with factors such as droplets size, electrical conductivity, drug content, pH and flow properties were relatively held constant in order to ensure the abilities of these systems to exert the expected effects.

Materials and Methods
Materials
Disodium hydrogen phosphate, potassium dihydrogen phosphate and sodium hydroxide were provided by R & M Chemicals, England. Orthophosphoric acid and hydrochloric acid were supplied by BDH, England. Methanol and acetonitrile (HPLC grade) were purchased from J.T. Baker, USA. Nylon membrane filters (0.45 μm pore size) was purchased from Whatman International, England. Palm oil esters (POEs) was a gift from Universiti Putra Malaysia (UPM), the co-researchers. Tween 80 and sodium benzoate were purchased from Sigma-Aldrich, Germany. Ibuprofen was supplied by Novaltek Life-science, Shanghai, China.

Methods
Before carrying out the three-month stability study, the tested formulations were subjected to precipitation test under accelerated condition at 40 ^{o}C for 15 days. Thereafter, three different temperatures (4, 25 and 40 ^{o}C) were used to perform the proposed stability studies. Accelerated studies were carried out by placing all samples in an oven at 40 °C. On the other hand, intermediate stability studies were conducted by keeping the samples in an air-conditioned room at 25 °C (room temperature). The last stability study was executed at 4 ^{o}C by placing the sample in the refrigerator. At periodic intervals of 15, 30, 45, 60 and 90 days, triplicate parallel determinations of samples droplets size, conductivity, drug content, pH and intrinsic viscosity were performed and compared to the initial values of respective measurements. [10]

Method of Preparation of Selected Nano-scaled Emulsions
Preparation process was conducted by initially blending specified ratios of the oil phase (POEs) and the emulsifier (Tween 80) in a beaker and mixing at a speed of 750 rpm using a low shear mixer equipped with three blades propeller and temperature control of 40 ± 1 °C for 30 min. Subsequently, 5% w/w ibuprofen was dissolved in the solution and the resultant mixture was further revolved at the same speed and temperature for another 30 min. The external phase (pH 7.4) comprising two separate proportions, a small part containing 0.20% w/w sodium benzoate, as a preservative, and a second large one having specific amounts of Carbopol$^®$ 940, as a viscosity modifier, was successively added drop by drop with continuous stirring for another 90 min. Agitation using the low shear mixer at a rotation speed of 1500 rpm was then used for approximately 4-5 hr to ensure the formation of homogenous nano-scaled emulsions.

Droplets Size Measurement
The droplets size of formulations G40, G45 and G47 was measured using Nanophox particle size analyzer, Sympatec GMBH, Germany and Malvern zeta sizer 1000 HAS, Malvern Works, UK. Both equipments compute and determine the globules size depending on the basic principle of photon correlation microscopy. In this technique, the Laser light beam diffracted by the droplets is detected by an image detector which processes the data to determine and record the droplets size. The limit of detection of these equipments ranges

between 1 nm and 1000 nm. The samples were diluted with the corresponding external phase to achieve a K count in the range of 50-200, as required by Malvern and Nanophox before performing the measurement. K count is a value that represents the number of particles contained in each sample. Light scattering was monitored at an angle of 90° and a temperature of 25 °C.

The mean droplets size of these formulations at the predetermined intervals was calculated and later compared to that of the freshly produced preparations to determine the change in droplets size over the period of observation.

Conductivity Measurement

The conductivity of formulations G40, G45 and G47 was determined using a conducto-meter (Cyberscan, Eutech instrument, Singapore). Two grams of each sample were placed in a beaker followed by immersing the conducto-meter probe up to the bottom of the container. These measurements were recorded in microsiemens (μs) and then compared to that of the freshly prepared samples at the specified time intervals and temperatures for the purpose of shaping any change in conductivity.

pH Measurement

A pH-meter (Cyberscan, Eutech instrument, Singapore) was utilized to measure the pH values of formulae G40, G45 and G47 stored at the determined temperatures over the specified time intervals. The pH-meter was calibrated before each use to measure the pH values of the produced emulsions. A specific amount equals to 2 gm of each sample was transferred into a beaker followed by dipping the pH-meter probe into the bottom of the container. These results were then compared to that of freshly prepared formulations to determine any change in samples pH values at the temperatures studied.

Rheological Measurement

The rheological properties of formulae G40, G45 and G47 were assessed using a rheometer (Rheologica instrument AB, Sweden). A cone-and-plate geometry (plate diameter 40 mm) was used and the experiment was conducted under the following conditions: about 0.5 gm of the sample

to be studied was placed on the plate and left to equilibrate at a controlled temperature (25 $\pm$ 0.1°C) for 3 min before bringing down the cone. This was done to ensure the thermal as well as the structural equilibration of all samples. Excess sample was removed using spatula and tissue papers. The shear stress was applied in an increasing manner at a rate of 5 pascal/2 sec and the shear rate measurements were recorded. [11] The experiment was repeated for other samples and triplicate trials were done for each of them. Rheograms were drawn by plotting shear stress on the x axis and shear rate on the y axis. Rheological parameters of the nano-scaled emulsions were calculated using the following equations. [6]

$$F^{N} = \eta^{G} \quad \ldots\ldots\ldots (1)$$
$$\log G = N \log F - \log \eta \quad \ldots\ldots\ldots (2)$$

Where G, F, N and η are shear rate, shear stress, exponential constant that defines the type of flow and viscosity coefficient, respectively. The intrinsic viscosity of the freshly prepared formulations was similarly calculated and then compared to that of the stored samples after specified time intervals and at different temperatures.

Drug Content Measurement

The amount of ibuprofen contained by formulations G40, G45 and G47 was analyzed using an HPLC method which was modified and previously validated by our research group. [12] One gram of each sample was dissolved in a mobile phase comprising acetonitrile: methanol: 5mM disodium hydrogen phosphate at a ratio of 52: 20: 28. The samples were diluted with the mobile phase and filtered before performing the analytical HPLC method.

Statistical Analysis

SPSS version 16 was utilized to determine the statistical difference between samples studied. One-way ANOVA test was performed to find out the difference between all parameters studied at the initial time and after 90 days of observation and at all storage conditions. Statistically, significant difference was considered at a value of ($P < 0.05$).

Results and Discussion

Droplets Size Measurement

The data presented in table 1 demonstrate a non-significant change in the measured droplets size of all formulations (G40, G45 and G47) stored at different temperatures and analyzed at various time intervals compared to their initial sizes. These outcomes indicated that coalescence or aggregation of the dispersed droplets did not take place significantly.

concentration in emulsions preparation leads to an increase in surfactant film around the dispersed phase droplets causing the steric hindrance to rise, hence preventing coalescence. [13]

Many researchers reported a decrease in the ripening rate of emulsions droplets upon increasing the amount of surfactant used. [7, 14] It has been assumed that if oil is dissolved in surfactant micelles, the oil is then contained by the micellar system and is not susceptible to be

Table 1: Droplets size measurement in nm of formulations G40, G45 and G47 subjected to stability testing at different temperatures for specified time intervals

Storage	Droplets size measurement after specified days of storage					
temperature	0	15	30	45	60	90
G40						
4 °C	20.8 ± 0.1	20.8 ± 0.5	20.8 ± 0.6	20.9 ± 0.6	20.9 ± 0.5	21.0 ± 0.1
25 °C	20.8 ± 0.1	20.9 ± 0.4	20.9 ± 0.2	21.0 ± 0.6	21.1 ± 1.1	21.2 ± 0.1
40 °C	20.8 ± 0.1	20.9 ± 0.5	20.9 ± 0.5	21.0 ± 0.3	21.2 ± 0.3	21.3 ± 0.4
G45						
4 °C	176.0 ± 1.6	176.2 ± 0.3	176.7 ± 0.8	177.6 ± 0.6	178.1 ± 0.6	178.4 ± 0.7
25 °C	176.0 ± 1.6	176.5 ± 0.4	176.9 ± 0.4	177.4 ± 0.1	178.1 ± 0.9	178.5 ± 0.9
40 °C	176.0 ± 1.6	176.7 ± 1.0	177.2 ± 0.8	178.2 ± 0.9	178.5 ± 0.4	178.8 ± 0.7
G47						
4 °C	175.8 ± 1.0	175.9 ± 0.6	176.0 ± 0.7	175.8 ± 1.0	176.2 ± 1.7	176.3 ± 0.1
25 °C	175.8 ± 1.0	175.9 ± 0.7	175.9 ± 0.6	176.0 ± 0.8	176.2 ± 1.6	176.4 ± 1.0
40 °C	175.8 ± 1.0	176.0 ± 0.6	176.1 ± 0.6	176.3 ± 1.1	176.3 ± 0.7	176.5 ± 0.8

All data is presented as mean ± SD, (n = 3)

Stability of biphasic system can be further confirmed by the minimal increase in droplets size. Insignificant rise in droplets size under the accelerated or stressed conditions is almost always associated with the least free energy available in the system. This makes it the least susceptible to the effect of Ostwald ripening and coalescence. High surfactant concentration used in producing these nano-scaled emulsions may be held responsible for their stability. Increasing surfactant

dispersed directly in the continuous phase. As a result, such oil is not subjected to the same mass transfer between the dispersed droplets as when they are outside the micellar system. Therefore, the micelles of these systems withdraw the oil from the continuous aqueous phase to be reserved inside causing the ripening rate to decrease due to the low solubility of the oil in water. Similar results were reported in the preparation of emulsions comprising palm oil as the oil phase. [13]

Conductivity Measurement

Table 2 illustrates the measured conductivity of all formulae evaluated at the specified temperatures and time intervals. Initially the conductivity values of formulations G40, G45 and G47 were 557 ± 3.60, 550 ± 1.00 and 552 ± 1.73 µs, respectively. From the data presented in table 2, it is apparent that these values did not change significantly after three months at all temperatures used.

The conductivity measurements were made at the

insignificant changes in conductivity may point out to the absence of creaming or sedimentation in the produced nano-scaled emulsions over the period of observation. This stabilization effect may be attributed to the relatively comparable densities of POEs (the dispersed phase) and aqueous solution pH 7.4 (the dispersion medium) which were 0.8553 gm/cm^3 and 0.997 gm/cm^3, respectively. [15] Additional factors that contribute to the stability of the produced emulsions are the expected co-surfactant activity of ibuprofen and

Table 2: Conductivity measurements in µs of formulations G40, G45 and G47 subjected to stability testing at different temperatures for specified time intervals

Storage temperature	Conductivity measurement after specified days of storage					
	0	15	30	45	60	90
G40						
4°C	557 ± 3.61	559 ± 3.46	558 ± 2.65	559 ± 1.00	560 ± 2.65	561 ± 2.65
25°C	557 ± 3.61	558 ± 3.61	559 ± 3.00	560 ± 1.00	560 ± 1.00	561 ± 1.00
40°C	557 ± 3.61	558 ± 1.73	559 ± 1.73	561 ± 1.00	561 ± 2.65	562 ± 1.00
G45						
4°C	552 ± 1.73	552 ± 2.00	552 ± 2.00	552 ± 3.60	552 ± 1.73	553 ± 1.00
25°C	552 ± 1.73	551 ± 1.00	553 ± 1.00	553 ± 2.00	552 ± 3.60	551 ± 2.65
40°C	552 ± 1.73	553 ± 1.73	554 ± 1.00	554 ± 1.00	554 ± 1.00	554 ± 2.00
G47						
4°C	550 ± 1.00	550 ± 1.73	549 ± 2.00	550 ± 2.65	551 ± 2.00	551 ± 1.00
25°C	550 ± 1.00	549 ± 1.73	549 ± 1.00	551 ± 5.29	552 ± 2.65	552 ± 2.65
40°C	550 ± 1.00	551 ± 4.58	549 ± 1.00	551 ± 1.00	552 ± 1.73	552 ± 1.00

All data is presented as mean ± SD, (n = 3)

bottom of the container. A non-significant change in these measurements indicates that the bottom of the container maintains the same amount of oil phase within the time intervals specified for the stability study. Basically, separation of emulsion phase and the subsequent upward movement of the oil phase is concerned with the enhancement in the conductivity at the bottom of the emulsion container as a result of the lesser interference from the lower number of the oil droplets. These

the nano-meter range of the dispersed phase droplets. [16]

pH Measurement

The measurements of the pH values of freshly prepared formulations presented in table 3 showed insignificant change after three months of observation at storage temperatures of 4, 25 and 40 °C. This perhaps indicates that ionization and hydrolysis of the various ingredients included had

not occurred significantly over the examination period.

Rheological Measurement
The assessed rheological characteristics of formulations G40, G45 and G47 shown in table 4 demonstrated an insignificant change in the values of calculated intrinsic viscosity at all temperatures studied after three months of storage compared to their primary values.

The polyoxyethylene surfactants, like Tweens, have 20 polyoxyethylene groups in their chemical structure. Such a composition allows them to be easily dispersed in water via the formation of hydrogen bonds between water molecules and these polyoxyethylene groups. [17] Such orientation renders them capable of forming a network mainly composed of these polyoxyethylene chains. Therefore, these unchanged viscosities may be attributed to the

Table 3: pH measurement of formulations G40, G45 and G47 subjected to stability testing at different temperatures for specified time intervals

Storage temperature	pH measurement after specified days of storage					
	0	15	30	45	60	90
G40						
4 °C	6.83 ± 0.02	6.83 ± 0.01	6.82 ± 0.02	6.82 ± 0.02	6.81 ± 0.01	6.81 ± 0.02
25 °C	6.83 ± 0.02	6.82 ± 0.03	6.81 ± 0.02	6.81 ± 0.01	6.80 ± 0.02	6.80 ± 0.02
40 °C	6.83 ± 0.02	6.81 ± 0.01	6.80 ± 0.01	6.79 ± 0.02	6.79 ± 0.02	6.79 ± 0.02
G45						
4 °C	6.81 ± 0.02	6.81 ± 0.01	6.81 ± 0.01	6.81 ± 0.01	6.80 ± 0.01	6.79 ± 0.01
25 °C	6.81 ± 0.02	6.81 ± 0.01	6.80 ± 0.01	6.81 ± 0.01	6.80 ± 0.01	6.79 ± 0.02
40 °C	6.81 ± 0.02	6.81 ± 0.01	6.80 ± 0.03	6.80 ± 0.03	6.79 ± 0.01	6.79 ± 0.01
G47						
4 °C	6.81 ± 0.02	6.81 ± 0.02	6.80 ± 0.01	6.80 ± 0.02	6.80 ± 0.03	6.79 ± 0.01
25 °C	6.81 ± 0.02	6.81 ± 0.01	6.81 ± 0.01	6.80 ± 0.02	6.79 ± 0.01	6.79 ± 0.01
40 °C	6.81 ± 0.02	6.81 ± 0.01	6.81 ± 0.01	6.80 ± 0.01	6.79 ± 0.01	6.79 ± 0.01

All data is presented as mean ± SD, (n = 3)

Table 4: Intrinsic viscosity measurement in poise of formulations G40, G45 and G47 subjected to stability testing at different temperatures for specified time intervals

Storage temperature	Viscosity measurement after specified days of storage					
	0	15	30	45	60	90
G40						
4 °C	11.80 ± 0.13	11.22 ± 0.88	11.27 ± 0.68	11.29 ± 0.32	11.44 ± 0.40	11.11 ± 0.52
25 °C	11.80 ± 0.13	11.71 ± 0.05	11.14 ± 1.32	11.53 ± 1.08	11.59 ± 1.33	11.20 ± 0.91
40 °C	11.80 ± 0.13	11.55 ± 0.50	11.78 ± 1.31	11.17 ± 1.87	11.73 ± 1.13	11.71 ± 1.45
G45						
4 °C	148.00 ± 7.36	147.17 ± 7.36	148.40 ± 1.04	147.07 ± 4.24	146.53 ± 3.94	146.08 ± 5.43
25 °C	148.00 ± 7.36	148.11 ± 4.04	147.83 ± 2.33	147.12 ± 2.83	146.04 ± 2.49	145.43 ± 3.52
40 °C	148.00 ± 7.36	147.89 ± 5.56	147.07 ± 3.81	146.11 ± 7.27	145.70 ± 5.72	144.78 ± 3.99
G47						
4 °C	148.00 ± 7.36	148.70 ± 5.17	147.36 ± 4.51	146.80 ± 2.97	146.21 ± 4.95	145.99 ± 2.38
25 °C	148.00 ± 7.36	147.13 ± 1.81	146.51 ± 2.96	146.05 ± 3.61	145.92 ± 0.95	145.19 ± 1.17
40 °C	148.00 ± 7.36	146.89 ± 4.18	146.06 ± 3.96	145.62 ± 2.33	145.10 ± 1.67	144.91 ± 1.97

All data are presented as mean ± SD, (n = 3)

intactness of these hydrogen bonds between these chains themselves and with the water molecules over the time frame of stability study.

Tween 80 has a cloud point of about 700 °C [18], which makes it extremely stable and unexpected to show any rheological changes when it is exposed to lower temperatures, for instance 40 °C and below. Form these results, it can also be suggested that there was minimal water evaporation, which contributed to the stability of the emulsions produced.

Additionally, formulae G45 and G47 were rheologically modified using Carbopol® 940, a polymer that is able to form a gel network that can add to the total product stability. Carbopol® 940 can form a well organized network at the concentration utilized in these two formulations. Thus, the calculated intrinsic viscosity of these formulae did not show any significant change over the period of observation.

Drug Content Measurement

Table 5 shows that the determined ibuprofen content in all samples evaluated was in the range of 98-101%. At all the conditions used in our study, the comparison of these values with the initial drug concentration demonstrated a non-significant change after 3 months of observation.

Unchanged drug concentration alongside with the unchanged pH values of these formulae indicates an insignificant change in the ionization or degradation of the drug under the tested circumstances.

Table 5: Drug content measurement in percentage of formulations G40, G45 and G47 subjected to stability testing at different temperatures for specified time intervals

Storage temperature	Ibuprofen content measurement after specified days of storage					
	0	15	30	45	60	90
G40						
4 °C	100.05 ± 1.20	99.70 ± 1.20	99.56 ± 1.18	99.50 ± 1.48	100.05 ± 0.91	98.96 ± 0.89
25 °C	100.05 ± 1.20	99.81 ± 1.68	99.77 ± 1.97	99.14 ± 0.34	98.23 ± 1.61	97.90 ± 2.36
40 °C	100.05 ± 1.20	99.17 ± 0.29	99.35 ± 1.17	98.56 ± 0.73	98.27 ± 0.56	97.77 ± 1.31
G45						
4 °C	100.18 ± 0.57	99.35 ± 1.17	98.56 ± 0.73	98.61 ± 2.10	98.31 ± 2.37	97.90 ± 0.38
25 °C	100.18 ± 0.57	99.59 ± 0.64	99.07 ± 0.10	98.95 ± 0.56	98.48 ± 2.41	98.23 ± 0.19
40 °C	100.18 ± 0.57	100.07 ± 0.83	99.56 ± 1.41	100.05 ± 0.91	99.19 ± 0.26	99.07 ± 1.63
G47						
4 °C	100.20 ± 1.13	99.47 ± 0.77	98.75 ± 0.81	98.34 ± 0.61	98.09 ± 2.81	97.99 ± 0.96
25 °C	100.20 ± 1.13	100.71 ± 1.07	99.07 ± 0.26	98.55 ± 1.78	98.36 ± 2.44	98.25 ± 0.93
40 °C	100.20 ± 1.13	100.92 ± 0.73	100.16 ± 0.64	99.64 ± 0.76	98.89 ± 1.10	98.52 ± 0.74

All data are presented as mean ± SD, (n = 3)

Conclusions

Data from the present work convincingly demonstrated that our nano-scaled emulsions comprising ibuprofen, as an active ingredient, at a concentration of 5% w/w were stable against creaming, coalescence, phase separation and Ostwald ripening and were successfully produced. Basically, these formulae consisted of TEA aqueous solution pH 7.4, POEs and Tween 80 at a ratio of 37:25:38. The stability of these formulations can be mainly ascribed to the non-ionic type of surfactant used as an emulsifier and to Carb 940 utilized in some of them as a rheology modifies. Similar results were obtained by [19], where Tween 80 was used in stabilizing the produced celecoxib nano-emulsions. This indicates the potency of non-ionic surfactants, particularly Tween 80 in producing stable nano-scaled emulsions.

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