



International Journal of Biopharmaceutics

Journal homepage: www.ijbonline.com

IJB

FORMULATION AND EVALUATION OF INNOVATIVE GLIBENCLAMIDE NANOEMULSION FOR IMPROVED THERAPEUTIC OUTCOMES IN TYPE 2 DIABETES MELLITUS

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ABSTRACT

The objective of the current research effort was to develop and characterize Glibenclamide (GCL)-loaded nanoemulsions to achieve a better therapeutic effect in Type 2 Diabetes Mellitus treatment. Different oils, surfactants, and co-surfactants were used to make the nanoemulsions and the formulation was optimised with respect to enhanced solubility, stability and drug release characteristics. Spectrophotometric analysis indicated that GCL was uniformly incorporated in the formulations with 229.5 nm as the 239.5 nm. The solubility investigations indicated that GCL was most soluble in ACC 200 E6, whereas the compatibility of the selected surfactants and co-surfactants (Cr RH40 and T80) with the drug was good. The formulations were physically stable as determined by stability tests (centrifugation, heating-cooling and freeze-thaw cycles). The optimized formulations (F1-F6) exhibited drug release efficiency (DE) of 45.78-59.33 percent and t₅₀ percent of 2.43-6.44 hours. The findings show that the nanoemulsions have a possibility of being used as transdermal drug administration system in the management of Type 2 Diabetes Mellitus.

Key words: Glibenclamide, Type 2 Diabetes Mellitus, Nanoemulsion, Drug Release.

INTRODUCTION

Drug molecules are transported using nanoemulsions, a colloidal particulate system with submicron particles. Nanometers are between 10 and 1,000 nm in size. Solid sphere carriers with negative charges are characterized by amorphous and lipophilic surfaces. Drug delivery systems are effective in improving the effectiveness and reducing the side effects of drugs (Karthik P., *et al.*, 2017). An emulsion is a two-phase system where one of the phases is dispersed intimately in another phases as droplets with diameters in the range of 0.1 to 100 nanometers. Even a thermodynamically unstable system can be stabilized due to the existence of an external source of energy (Qian C., *et al.* 2011).

The dispersed phase can also be referred to as the internal phase, discontinuous phase and the dispersion medium can also be referred to as external phase, continuous phase or dispersion medium. Drugs and bioactive food components are currently administered via lipid-based formulations due to their low oral bioavailability (Feeney O.M *et al.*, 2016). A nanoemulsion has a high interfacial region and is stable, protecting compounds against harsh environmental conditions and enhancing their performance (Madene A *et al.*, 2006). A wide range of biopharmaceuticals, including vaccines, DNA-encoded drugs, antibiotics, and DNA-encoded drugs, are delivered in this form (Shakeel F *et al.*, 2007). As compared with other dosage forms, this technology allows the formulation to be delivered orally, ocularly, and transdermally (Gasco M.R *et al.*, 1991). One can add castor oil, corn oil, coconut oil, evening primrose oil, linseed oil, mineral oil, olive oil, peanut oil and so on., to nanoemulsions. Nanoemulsions contain various

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surfactants (ionic and non-ionic) of varying characteristics (Kriwet K *et al.*, 1995).

Nano Emulsion

Compared to ordinary emulsions or microemulsions, nanoemulsions are translucent. Nanoemulsions are colloidal dispersions of two immiscible liquids that are thermodynamically unstable. Nanoemulsions consist of dispersed phases and dispersing mediums formed by different liquids. An emulsion of nanoparticles is composed of droplets with diameters ranging from 10 to 200 nanometers. Negatively charged solid sphere carriers are covered by amorphous, lipophilic surfaces. The use of magnetic nanoparticles can enhance site specificity. It is possible to stabilize this thermodynamically unstable system emulsifying agent (emulgent or emulsifier) through the presence of a substance. The dispersed phase can also be referred to as the internal phase or the discontinuous phase, and the outer phase as dispersion medium, external phase or continuous phase. The emulsifying agents are also termed as intermediates or interphases (Tiwari S.B *et al.*, 2006)]. A nanoemulsion can as well be non-technically called a miniemulsion which is a fine dispersion of oil/water or water/oil, stabilized by an interfacial film of surfactant molecules with a droplet size range of between 20 and 600 nanometers. Since nanoemulsions have a small size, they are transparent. (McClements D.J *et al.*, 2012)

Nanoemulsions are of three types (a) oil in water nanoemulsions where the oil is dispersed in the continuous aqueous phase, (b) water in oil nanoemulsions where water forms the dispersed phase in the continuous oil phase and (c) bicontinuous nanoemulsions. Nanoemulsions are among the most efficient methods to get active ingredients to their destination sites, and they have gained much interest over the past years due to their numerous applications. Nanoemulsions can be delivered by multiple routes, such as oral, topical, and parenteral (Baboota S., *et al.*, 2007). Nanoemulsions are defined as thermodynamically stable solutions of non-soluble liquids stabilized by interfacial surfactant films. It consists of an oil and water emulsion system with droplet sizes ranging from 50 to 1000 nanometers.

MATERIALS AND METHODOLOGY

Glibenclamide Stock solution was prepared by weighing 50 mg of the drug substance and dissolving it in ethanol in a 50 ml volumetric flask and bringing the volume up to the mark. To a 100 ml volumetric flask, 2.0 ml of this solution was added and the volume was made up with alkaline borate buffer (pH 9.5) to give a final concentration of 20 µg/ml. A blank solution was done likewise but without the drug. To prepare the calibration curve, the stock solution was diluted to create a series of dilutions between 2 and 12 (2 micrograms per milliliter) in steps of 2 (that is, 2, 4, 6, 8, 10, 12 micrograms per milliliter), and 0.1 ml of concentrated hydrochloric acid

was added to each dilution. It was observed that when the concentration of hydrochloric acid was added beyond 12 micrograms per milliliter, Glibenclamide started precipitating probably because of low solubility at low pH. Hydrochloric acid was also added in the same proportion to the blank solution. λ_{max} of Glibenclamide was found to be 229.5 nm and standard calibration curve was plotted by reading the absorbance of the prepared dilutions against the blank at this wavelength.

To study solubility, an excess amount of Glibenclamide was placed in oils (Capryol 90, isopropyl myristate, oleic acid, olive oil, sunflower oil and linseed oil), surfactants (Tween 20 and Tween 80) and co-surfactants (Transcutol P, propylene glycol, PEG 400 and glycerol) in individual stoppered vials. A cyclic mixer was used to vortex the mixtures and equilibrate them in an orbital shaker at 25 $\pm$ 1.0 $^{\circ}$ C over 72 hours. following equilibrium, the mixtures were centrifuged at 3000 rpm, 15 minutes and the supernatant filtered using 0.45-µm membrane. The filtrates were dissolved in appropriate solvent and diluted with pH 9.5 buffer and measured in UV-visible spectrophotometer at 229.5 nm to find out the concentration of Glibenclamide.

A series of stress tests were used to evaluate thermodynamic stability of formulations of interest. These consisted of a heating cooling cycle, in which formulations were subjected to six cycles of 4 $^{\circ}$ C to 45 $^{\circ}$ C with a 48-hour hold at each temperature, followed by visual evaluation of instability. To test the phase separation, centrifugation was done at 3500 rpm, 30 minutes. Finally, the formulations were subjected to freeze thaw by alternating between -21 $^{\circ}$ C and + 25 $^{\circ}$ C and observed to determine any form of instability like precipitation or phase separation hence physical stability of samples under stress conditions. (Anton N *et al.*, 2008)

Evaluation of Glibenclamide Nano emulsion

The particle size analysis of nanoemulsion formulation was done by dispersing 0.1 ml of sample into 50 ml of distilled water in a volumetric flask and then mixing it gently by inverting the flask. A particle size analyzer (Horiba) was used to measure the average globule size on the basis of light scattering fluctuations owing to Brownian motion; the measurements were performed at 25 $^{\circ}$ C and 90 $^{\circ}$ angle. Determination of the zeta potential was done in the same way, which gave information about the surface charge and emulsion stability. A UV-Visible double-beam spectrophotometer was used to determine the percent transmittance of the nanoemulsion at 560 nm with distilled water acting as the blank. The viscosity was determined by Brookfield viscometer (LVDV-II+P) with S-34 spindle and 25 $^{\circ}$ C with 10 ml sample volume. The formulations were studied at various spindle speeds (5 100 rpm) and rheograms were drawn to examine the shear stress verses shear rate and to determine the rheology of the system.

The dialysis bag method was used to determine in-vitro drug release of Glibenclamid nanoemulsion. The formulation containing 2.5 mg of Glibenclamide in 1 ml sample was put into a dialysis bag and incubated in 50 ml of 0.1N HCl during the first 2 hours, followed by the addition of pH 7.4 buffer, and both were kept at 37 °C. A magnetic stirrer was used to constantly stir the medium. Samples were taken at pre-set time points and equal volume of fresh medium was added to keep the conditions at sink conditions. A UV-Visible spectrophotometer was used to determine the drug concentration in the collected samples at a wavelength of 275 nm. Also, the compatibility of drug-excipient was done by Fourier Transform Infrared (FTIR) spectroscopy using SHIMADZU instrument. To check any possible interaction and to ascertain that the chemical stability of Glibenclamide is maintained in the formulation, the samples were scanned between wavelengths of 400 to 4000 cm⁻¹.

RESULT

Glibenclamide (GCL) and oleic acid (OA) emulsion formulation was realized by changing the ratio of oil, surfactant and co-surfactant, maintaining the quantity of GCL as constant. Out of the many formulations that were made, some specific nanoemulsions were selected owing to the critical responses of clarity, homogeneity as well as physical stability. A spectrophotometric method was also optimized to screen the samples by estimating the concentration of GCL in methanol, and the λ_{max} was determined to be 300 nm. The optimum nanoemulsion formulation needed excipients that possess finest solubilizing power so that drug is not precipitated out and final product is clear, transparent, single phase liquid at room temperature. In the compatibility screening, the compatibility of numerous oils, surfactants, and co-surfactants with the drug was confirmed by the fact that their presence did not cause a significant drop in GCL concentration, and did not interfere with spectrophotometric analysis. Of all the oils screened, ACC 200 E6 was found to have the greatest solubility to GCL and as such was chosen as the oil phase. Also, Cr RH40 and Tween 80 displayed favorable solubility performances and were selected as the co-surfactant and surfactant, respectively.

The selected formulations were also rigorously tested to determine the dispersion and thermodynamic stability which are major properties of nanoemulsions. These consisted of centrifugation to determine phase separation, heating cool and freeze thaw cycles to represent storage at stress conditions. Nanoemulsions prepared at proper composition of oil, surfactant and water did not show any physical instability during these experiments by remaining unaffected by creaming, cracking or phase separation. The experimental outcomes

ensured that the chosen formulations had superior dispersion stability and recommended contenders to proceed with the further development.

Evaluation of true nanoemulsion

Drug Content

Drug content was also not significantly different in formulation F1 and F6 regardless of the compositional differences. The drug content fell between 99.36 to 100.56% indicating that there was uniform distribution of GCL in the formulations.

Spectroscopic Absorbance

It can be expected that, except in the special case of cloudier solutions, the absorbances will be lower in optically clear solutions than in cloudier solutions since, in the cloudier solutions, a larger fraction of incident radiation will be scattered and, in the special case of cloudier solutions, a larger fraction of incident radiation will be scattered. It has been assumed that dispersions of aqueous solutions, of small absorbances, are optically clear, whilst the optical clarity of drops of oil depends upon their fine dispersion. To determine the optical clarity of a particular solution quantitatively, spectrophotometers were employed so as to measure the extent of the light of specific wavelength that is transmitted by the solution at a particular wavelength. When comparing the absorbances of formulations F1-F6 after dilution with distilled water and pH 7.4 PB at the different time points after the dilution with distilled water and pH 7.4 PB, respectively. This indicates that formulations F1-F6 were stable within 24 hours because there was no change in absorbance values.

Photon correlation spectroscopic studies

The key property of nanoemulsions that determines the rate and extent of drug release and efficacy of drug absorption is the droplet size that is in the order of nanometers. A smaller size of the droplets is relatively accompanied with a better bioavailability and rapid uptake velocity of the drugs. This study was aimed at vindicating that the emulsions so made were nanoemulsions, based on the analysis of their droplet size distributions. Such an analysis not only confirmed the classification of nanoemulsions but also gave critical information to optimise the formulation relative to the dynamic of the particle size. It was also seen that the droplet size was constant at different proportions of oil, surfactant and co-surfactant, when diluted in both distilled water and phosphate buffer at pH 7.4. It was exemplary that formulations F1 to F6 showed no notable increment in mean particle size even after 24 hours of post-dilution in the various media, which portrays high structural integrity and stability of the emulsions across conditions.

Zeta Potential Determination

Table indicates the zeta potentials of the nanoemulsion formulations with and without OA. Our data show a wide distribution of zeta potential of the formulations F1-F6 without OA, the values being -6.26 mV to -14.35 mV. The negative zeta potential of the emulsion droplets formed is attributed to the free fatty acids that exist in these formulations since they contain fatty acids. Nevertheless, along with the addition of OA, which is a positive charge inducer, all formulations acquired a positive zeta potential, with the range of +15.90 to +24.80 mV, indicating that the electrostatic attraction caused by positivity induced by OA led to an increase in the adhesion of the droplets to the cell surface.

Evaluation of nanoemulsion gel

The analysis of the formulations (F1-F6) by drug content in the transdermal nanoemulsion gel formulations was found to be 99.12- 100.32% which indicated that Glibenclamide (GCL) was well distributed within the gel matrix. Such consistency also indicates that the gelling process did not affect the drug distribution, and therefore, the homogeneity of the formulation was maintained. pH values of the nanoemulsion gels were found to be within the range of 5.18-5.48, a little lower but still close to the natural pH of the skin (5.5-6.0). This near resemblance determines the suitability of the formulations to the skin, with chances of causing minimal irritation as a probability when applied. determinations of viscosity, summerized in Table 5, were made undiluted. It was observed that at constant concentration of the oil phase ACC 200 E6 the viscosity decreased (745.14 to 563.27 %) with the decrease in concentration of the surfactant Cr RH40. More so, it was realized that as the concentration of ACC 200 E6 was increased, the viscosity reduced further. These results indicate how the ratios of oil and surfactants play a crucial role in the rheological behavior of the nanoemulsion gels, which is guaranteed to ascertain desired application and drug release profile in transdermal delivery applications.

In vitro release studies

Six formulations of nanoemulsion gels (F1-F6) were identified to be able to release the same amount of active pharmaceutical ingredient and their profiles were represented in Figure 3. In this respect it was suggested that an optimal formulation would be optimised on a basis of maximising DE and minimising t50%. Regarding the DE range of 45.78 to 59.33%, t50% was found to be between 2.43 to 6.44 hours in case of nanoemulsion gels (F1-F6). It was observed that at constant level of ACC 200E6 (F1-F3), t50%. reduces by 6.44 to 4.21 hr,

whereas DE values augments by 45.78 to 51.57 %. It could be because of a drop in viscosity between F1 to F3. The same was observed with the transdermal nanoemulsion gels F4-F6 which were likely to experience a reducing consistency due to a reducing consistency.

Compatibility studies

Besides physical characteristics of a drug, there are several factors that are used to determine the efficiency of its delivery system. It is necessary to point out here that, when we talk of compatibility of a drug with an excipient we are talking of their solubility and /or interaction without making any change in the chemical nature of either the drug or the excipient. Taking into account the fact that each drug possesses individual chemical and physical properties, a delivery, prepared as a result of a specific excipient, will not be universal to carry all the drugs, since each drug has individual chemical and physical properties. The analysis of pure drug, pure excipient, and their PMs and CMs by FTIR and DSC was employed to understand the possible drug-excipient interaction.

Fourier transforms infrared spectroscopic studies

A series of infrared spectra were taken so as to establish whether there could be any drug-excipients interactions. Figure 6 display IR spectra of glibenclamide, single excipients, physical mixtures (PMs) and co-melts (CMs) of the drug with single excipients, along with their respective IR spectra. Figure 4 shows that the spectral data reveal that the characteristic absorption of the drug is retained in the 1:2 physical mixtures (PMs) and co-melts (CMs) with each excipient. FTIR Spectrum of pure GCL exhibited typical amide I, II and III peaks at 3367.82, 3315.74 and 1716.70 -1 cm, urea carbonyl stretching (urea N-H stretching) vibrations at 1618.33 and 1525.74 -1 cm-1; and SO2 stretching vibrations at 1161.19 and 1342.50 -1 cm-1.

Differential scanning calorimetric Studies

A DSC was employed in the detection of formulation incompatibilities as a result of the drug-excipient interaction. Figure 5 displays three DSC thermograms representing the thermograms of pure glibenclamide, its excipients (ACC 200 E6, Cr RH40 and T-80), the physical mixtures of these, and the co-melt of both at a ratio of 1:2 (drug: excipient). The melting point depression has resulted in the peaks of PM and CM of GCL-Cr RH40 shifting to lower temperature (158.19oC and 158.79oC, respectively). This has been also observed in other studies.

Preparation of nanoemulsions

Table 1: Composition Of Glibenclamide Nanoemulsion

Ingredients	F1	F2	F3	F4	F5	F6
Glibenclamide	0.012	0.012	0.012	0.012	0.012	0.012
Carbopol 940	0.05	0.05	0.05	0.05	0.05	0.05
Acconon 200	0.10	0.10	0.10	0.30	0.30	0.30
Cremophore	0.72	0.49	0.18	0.56	0.35	0.14
Tween 80	0.18	0.49	0.72	0.14	0.35	0.56
Oleylamine	0.05	0.05	0.05	0.05	0.05	0.05
Triethanolamine	0.025	0.025	0.025	0.025	0.025	0.025
Distilled Water	5.0	5.0	5.0	5.0	5.0	5.0

Table 2: Dispersion stability studies

Code	ACC 200 E6 (gm)	GCL (gm)	Cr RH40 (gm)	T-80 (gm)	Cr RH40: T-80	OA(gm)
F1	0.012	0.10	0.72	0.18	4:1	0.01
F2	0.012	0.10	0.495	0.495	1:1	0.01
F3	0.012	0.10	0.72	0.72	1:4	0.01
F4	0.012	0.30	0.14	0.14	4:1	0.01
F5	0.012	0.30	0.35	0.35	1:1	0.01
F6	0.012	0.30	0.56	0.56	1:4	0.01

Table 3: Dispersion stability studies

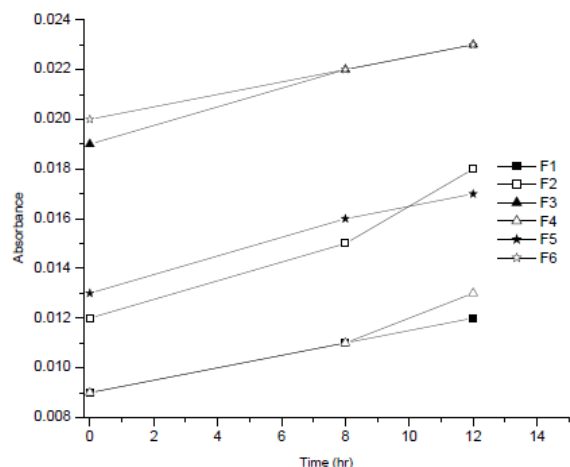
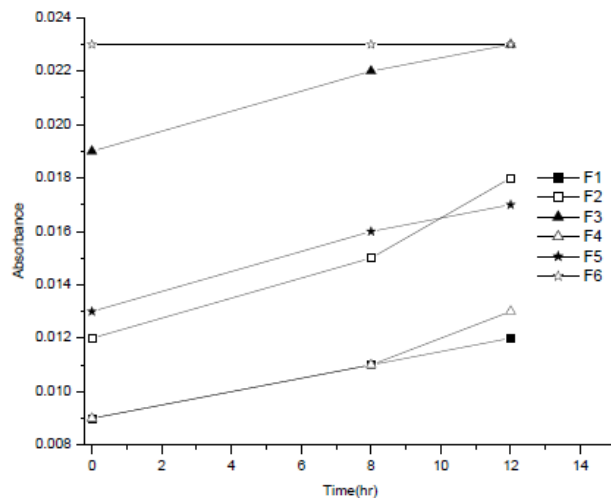
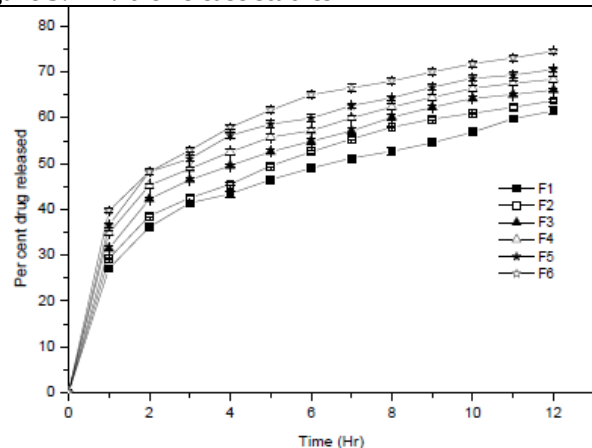
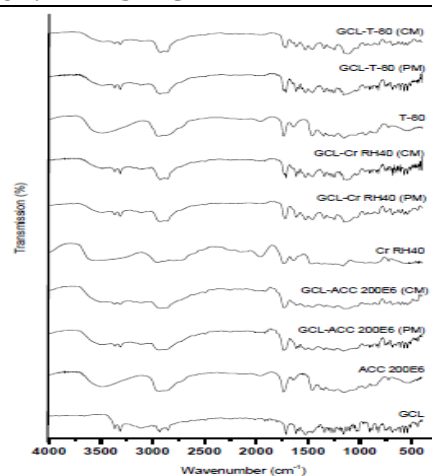
Code	Drug Content	Mean Particle Size (nm)			
		Distilled Water		PB (pH 7.4)	
		0 hours	24 hours	0 hours	24 hours
F1	99.73(0.46)	11.60(0.45)	12.65(0.15)	13.58(0.01)	13.89(0.18)
F2	100.56(1.33)	10.08(0.58)	11.47(0.77)	11.46(0.23)	12.56(0.18)
F3	99.36(1.42)	9.25(0.13)	9.28(0.33)	10.63(0.23)	10.98(0.40)
F4	100.12(1.32)	11.68(0.32)	12.70(0.94)	13.19(0.08)	14.26(0.18)
F5	99.81(1.03)	11.33(0.05)	13.13(0.30)	11.26(0.59)	12.82(0.24)
F6	100.32(1.94)	9.60(0.14)	10.18(0.56)	10.43(0.16)	10.75(0.06)

Table 4: Zeta Potential

Code	Zeta Potential (mV)	
	Without OA	Without OA
F1	5.30(1.30)	5.30(1.30)
F2	5.26(0.40)	5.26(0.40)
F3	-10.75(0.7)	-10.75(0.7)
F4	1.00(0.42)	1.00(0.42)
F5	0.19(1.29)	0.19(1.29)
F6	4.35(0.34)	4.35(0.34)

Table 5: Drug Content, pH

Code	Drug Content	pH	Viscosity (mPa)
F1	99.64 (0.43)	5.48(0.015)	745.14 (2.318)
F2	100.32 (1.24)	5.40(0.021)	721.13 (2.237)
F3	99.16 (1.38)	5.18(0.010)	563.27 (1.879)
F4	99.12 (0.86)	5.52(0.010)	610.19 (2.023)
F5	99.12 (0.86)	5.38(0.020)	570.89 (2.011)
F6	100.24 (1.94)	5.20(0.015)	520.58 (1.660)

Figure 1: The absorbance curves for formulations F1- F6 post-dilution with water are plotted versus time.**Figure 2: Graph plotting absorbance versus time for formulations F1-F6 post-dilution with PB of pH 7.4 for formulations F1-F6****Figure 3: In vitro release studies****Figure 4: FTIR SPECTRA**

DISCUSSION

Glibenclamide (GCL) and Oleic Acid (OA) were prepared with different proportions of oil, surfactants, and co-surfactants. The choice of formulation was dependent on a range of parameters which were stripped investigated so as to come up with the most efficacious composition of the nanoemulsion. An optimum spectrophotometric procedure which can be used to estimate the concentration of GCL in methanol was optimized. It was found that the λ_{max} wavelength was 300 nm and this value was taken further into analysis. The chosen type of oils, surfactants and cosurfactants did not significantly interfere with the GCL chemical analysis procedure since the drug concentration

decreased insignificantly. It indicates that the components of the formulation do not interfere with the potential of the method to measure GCL quantitatively (Suyal J *et al.*, 2017). Out of the screened oils, ACC 200 E6 had the best GCL solubility and hence was the favorite oil to be used in the formulation. In addition, Cr RH40 and T80 displayed a positive solubility to the drug and thus they were chosen as a surfactant and co-surfactant respectively. Nanoemulsions are associated with physical and thermodynamic stability. Because of the nanoemulsions unique properties, they are less likely to separate, cream or crack compared to conventional emulsions and their composition makes them generally thermostable. The ability to withstand dispersion was

determined by centrifugation, heating-cooling, and freeze-thaw stability testing of the formulations (Syed H.K *et al.*, 2016). The findings affirmed that nanoemulsions using the chosen levels of oil, surfactant and co-surfactant had superior stability, since no phase separation or other forms of instabilities were detected in the course of these tests.

The drug content in all the formulations (F1-F6) was also similar and ranged between 99.36 to 100.56 percent indicating that drug was evenly dispersed in the formulations. These findings show that drug loading procedure was effective and drug was properly introduced into the nanoemulsion system. An important parameter that defines the quality of nanoemulsions is optical clarity since a cloudier solution scatters more light and is more likely to exhibit increased absorbances. Formulations F1-F6 were diluted with distilled water and phosphate buffer (pH 7.4) and absorbance was measured. The data indicated that the formulations had an absorbance value that was constant with time, implying that the formulations were optically clear and stable during the 24 hour period. The size of the nanoemulsion droplets must fall within the nanometer range so as to assure optimum drug release and absorption. The size of the droplet of the formulations was measured by means of photon correlation spectroscopy (PCS). Dilution with distilled water or phosphate buffer at pH 7.4, did not result in significant changes in the particle size of the emulsions after 24 hours. Such consistency in droplet size indicates that the formulations are stable and that their efficacy in releasing the drug would not be affected by time. Zeta potential is a major signifier of stability of colloidal systems. (Bali V., *et al.* 2010) The nanoemulsions zeta potential was determined in the presence and absence of OA. In absence of OA, zeta potential of formulations F1-F6 was found to be -6.26 mV to -14.35 mV. The emulsions containing free fatty acids were ascribed to the negative zeta potentials. The addition of OA, a positively charging inducer however, brought the zeta potential to the positive range of +15.90 mV to +24.80 mV. This shows that OA was useful in increasing the electrostatic stability of the droplets so that they adhered more easily to the cells surfaces.

All formulations (F1-F6) of nanoemulsion gels had a uniform drug content ranging between 99.12 to 100.32%. This is an indication that the GCL was uniformly dispersed in the gel formulation, which guarantees consistency and uniformity in drug release. The nanoemulsion gel formulations were measured in terms of pH to make sure that they are skin compatible (skin pH is usually between 5.5 and 6.0). The pH of the

formulations was found to be between 5.18 and 5.52, which is quite close to the natural pH of the skin, thereby indicating that the formulations can be used transdermally without irritating the skin. Gel formulations: Viscosity is a critical parameter that requires attention with regard to application and spreadability of the product (Patel N.A *et al.*, 2009). The formulations (F1G-F6G) were measured regarding their viscosity, and the results ranged between 520.58 mPa to 745.14 mPa. The viscosity also had an inverse proportion to the concentration of Cr RH40 in that, as the concentration of ACC 200 E6 increased, the viscosity reduced. The trend implies that formulations containing more percentages of ACC 200 E6 were less resistant to flow and thus easier to apply.

Formulations F1-F6 were subjected to in vitro release and the data indicated that all the formulations could release the drug with time. Drug Release Efficiency (DE) was between 45.78 and 59.33 %, and t50% (time taken to release 50 % of the drug) was between 2.43 and 6.44 hours. The higher the concentration of ACC 200 E6 in the formulation, the lower was the t50% value and, hence, the faster was the release of the drug. This implies that the formulations that had more of this surfactant enabled a faster dissolution and absorption of the drug. Fourier Transform Infrared (FTIR) spectroscopy and Differential Scanning Calorimetry (DSC) were applied to study the interaction between the drug and excipients. The FTIR analysis indicated that no major interactions occurred between GCL and the excipients since the characteristic absorption peaks of GCL were observed in the formulations. DSC analyses showed that there were small alterations in melting points of the drug-excipient mixtures signifying that there were minor interactions. These findings are an indication that the drug-excipient mixtures are compatible which is key to the stability and activity of the final formulation.

CONCLUSION

The preparation and analysis of GCL-loaded nanoemulsions and nanoemulsion gels proved that it is possible to improve the stability and drug release properties of the formulations by using certain oils, surfactants, and cosurfactants. The optimized formulations possessed acceptable drug content, excellent solubility and stability, appropriate pH and viscosity suitable to transdermal application. The compatibility tests and in vitro release studies prove the efficacy of the formulations to be used potentially as therapeutics.

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