RESEARCH ARTICLE

Impact of Lipid Type and Ratio in Rizatriptan Benzoate Nanostructured Lipid Carrier

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ABSTRACT

Nanotechnology represents a magic wand to solve most problems related to improving drug efficiency, one of the most important of these problems is the drug's permeability through biological membranes. Rizatriptan benzoate was used for the treatment of acute migraine, it has poor permeability and is difficult to administer through the nose. This study aims to design a nanostructured lipid carrier containing rizatriptan benzoate as a trial to enhance its biological permeability. A high shear homogenization technique was utilized as a method of preparation; glyceryl monostearate and becs wax are used as solid lipids while oleic acid and castor oil were used as liquid lipids in different ratios. Particle size analysis, polydispersity index, zeta potential, entrapment efficiency, and loading efficiency were considered the main criteria for the evaluation, meanwhile, the *in-vitro* release test was done for the formulas having smallest particle size. Moreover, the infrared spectroscopy and differential scanning calorimetry (DSC) are investigated for the selected formula. The obtained outcome revealed a significant effect on the particle size and entrapment efficiency upon enhancing the ratio of liquid lipid. Furthermore, changing the type of solid and liquid lipid leads to a dramatic alteration in the criteria of evaluation, also biphasic release pattern was seen. The infrared spectroscopy shows an intact rizatriptan benzoate, while DSC revealed a change of drug molecule to an amorphous state. In conclusion, a high shear homogenization can be used to formulate a successful nanostructured lipid carrier with good physical properties.

Keywords: Rizatriptan benzoate, Migraine, Nanostructured lipid carrier.

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INTRODUCTION

Nanotechnology and nanoscience have a huge potential for usage in a variety of disciplines of research and applications. Norio Taniguchi, a physicist at the University of Tokyo in Japan, coined the word "nanotechnology" in 1974 to describe materials with nanoscale dimensions. Nano prefix is a Greek word that means dwarf. Nanotechnology is the branch of science that studies processes at the molecular level and on the nano length scale (*i.e.,* 10^{-9}). It has several advantages over traditional dosage forms, including better effectiveness, protection of the active component from tissue pH and enzyme, dose reduction, medication delivery management, longer circulation duration, enhanced intracellular access, lower toxicity, improved biodistribution, and greater patient compliance.[1]

Nanotechnology has received a lot of interest recently in several fields. The creation of nanoemulsions, liposomes, niosomes, solid lipid nanoparticles (SLN), and nanostructured lipid carriers for intranasal drug administration has been a major focus of study in the preceding decade. These systems are paired with enzymatic inhibitors, nasal absorption enhancers, and/or mucoadhesive polymers to increase formulation stability, nasal penetration, and retention time. Although it is unclear how these methods boost medication absorption, it's thought that transportation of encapsulated drugs across membranes and a longer retention time and improved stability may help. However, the results of these nanotechnology-based systems have proven highly encouraging.[2] Nanostructured lipid carrier (NLC) is the new progeny version of SLN, a type of lipid-based drug delivery system that Muller developed in 1999/2000. the first two products, Nanorepair Q_{10} cream and Nanorepair Q_{10} serum were launched in Munich, Germany, in 2005. The third product, nanolipid CLR restore, was introduced within six months. NLC is one of the nanocarriers with the quickest time from discovery to the market.[3] In comparison to nanoemulsions, NLCs can firmLy immobilize medicines

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and prevent particles from coalescing due to the solid matrix. Furthermore, in the solid phase, the mobility of the inserted drug molecules is greatly decreased. Moreover, as compared to SLNs, the liquid oil droplets in the solid matrix enhance drug loading capacity. Low toxicity, biodegradability, drug protection, controlled release, and the avoidance of organic solvents during manufacture are all benefits of NLCs over polymeric nanoparticles.[4]

Migraine is a common neurologic illness affecting an estimated 1 billion individuals worldwide, most female.[5] Triptans class which has seven oral triptans available for therapeutic remedy (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, and zolmitriptan) are considered as second-line treatments, these agents act on 5-hydroxytryptamine type 1B/D (5-$HT_{1B/D}$) receptor agonists. If three migraine episodes have gone untreated, patients are encouraged to switch from one oral triptan to another.[6]

Rizatriptan benzoate is a second-generation member of a class of drugs known collectively as the triptan, it was approved in 1998 and marketed in 5 and 10 mg dosages strengths and is available in conventional tablets and rapidly disintegrating wafer formulations. It is used for the acute treatment of the headache phase of migraine attacks and is not used for prophylaxis. Rizatriptan is given as the benzoate, and doses are expressed in terms of the base in which rizatriptan benzoate 14.53 mg is equivalent to about 10 mg of rizatriptan.[7] Rizatriptan is a 5-$HT_{1B/1D}$ receptor agonist. The presumed mechanism of action of rizatriptan is *via* the activation of postsynaptic 5-HT_{1B} receptors within cerebral and dural vessel walls, causing vasoconstriction and inhibition of trigeminal perivascular nerve terminals. In addition, activation of presynaptic 5-HT_{1D} receptors prevents the release of vasoactive neuropeptides and blocks depolarization of trigeminal axons, also it was believed to act centrally in the brainstem, thereby blocking the transmission of pain.[8]

The chemical name of rizatriptan benzoate is N, N-dimethyl-[5-(1H-1,2,4-triazole-1-ylmethyl)-1H-indole-3] ethanamine monobenzoate.[9] The chemical structure of rizatriptan is shown in Figure 1.

MATERIALS AND METHODS

Materials

Rizatriptan benzoate (RNB), glyceryl monostearate (GMS), and lecithin were purchased from Baoji Guokang Bio-Technology Co., LTD, China. Tween 80 was taken from SCRC, India. Oleic acid was obtained from Thomas baker, India, fenugreek oil, soyabean oil was bought from Falcon, India. Castor oil, beeswax, and peppermint oil from Loba Chemie Pvt. Ltd.,

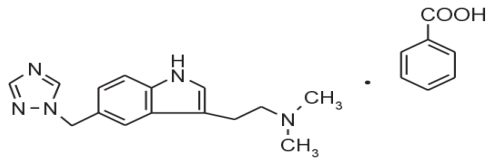

Figure 1: chemical structure of rizatriptan benzoate.

India. Sesame oil from Fluka AG. Chem., India. Palmitic acid was purchased from CDH, India. Stearic acid from Panreac appliChem, Spain. Deionized water purchased from AL Rafidain environment office for scientific, technical and industrial consultations, Iraq. All of the other material are of analytical grade.

Screening of Lipids

Solid Lipid Solubility of RNB

To achieve extreme drug loading, lipid screening was undertaken to select the best-suited lipid for RNB. Naked eyes were used under normal light to visualize the clear melted lipid with solubilized RNB to investigate its solubility in solid lipids, RNB was added to specified amounts of selected lipids (stearic acid, glyceryl monostearate, palmitic acid, beeswax), which were heated in 5 mL glass beaker to about 10°C above their melting point in a controlled temperature water bath.[10]

Screening of Liquid Lipids

To carefully select the most suited excipients for synthesizing required NLC, the solubility of RNB in different liquid lipids (Castor oil, oleic caid, aloe oil, soya bean oil, sesame oil, fenugreek oil) were established. In a typical procedure, an excess quantity of chosen medicine was combined with selected liquid lipids with the assistance of a hot plate magnetic stirrer to stir the mixture at 50 rpm for 24 hours at room temperature. The resulting mixtures were put aside for 72 hours, followed by centrifugation for 30 minutes at 1500 rpm. The samples were filtered via a 0.45 µm millipore filter. After that, 0.5 mL of supernatant was taken and diluted with a suitable volume of ethanol and evaluated utilizing UV spectrophotometer at 225 nm. For the manufacture of NLC, the liquid lipids with the greatest solubility were selected.[11]

Preparation of Rizatriptan Benzoate NLC

The nanostructured lipid carrier containing rizatriptan benzoate (RBN-NLC) was formulated using the modified high shear homogenization method using a high-speed homogenizer. Two solid lipids with valuable RNB solubility were used along with two types of liquid lipids (having a high value of RNB solubility) at a specified amount, 10 mg of the drug were added to a glass vial containing the lipids (solid and liquid) which were previously heated to a temperature about 10°C above the melting point of the solid lipid used. Meanwhile, the aqueous phase is prepared by the addition of the fixed type and concentration of surfactant to the 2 mL of deionized water, this phase is warmed up to the same temperature as the lipid phase. Then, the hot lipid phase was added drop by drop to the warmed aqueous phase. A pre-emulsion was constructed by stirring for five minutes using a hot plate magnetic stirrer. After that, the nanoemulsion was obtained by using a high-speed homogenizer at 20000 rpm for 20 minutes. Subsequently, the nanodispersion was set aside to cool at room temperature to solidify nanoparticles.[12]

Evaluation of the Rizatriptan Loaded NLC

The prepared formulas are investigated for the main nanostructured criteria to show the effect of various types and the ratio of solid and liquid lipid on the characters of the prepared NLC.

Particle Size Analysis

Dynamic light scattering (DLS) techniques were used to determine the particle size and polydispersity index of nanoparticles using a particle size analyzer (Zetasizer, Marvelon, UK) at a scattering angle of 90°C at room temperature, the sample was diluted tenfold with deionized water, and measurements were performed in triplicate for each sample.[13]

Zeta Potential

In nanodispersion, zeta potential is a physical characteristic. It is the differential charge between the bulk solution (dispersing medium) and the hydrodynamic shear surface (slipping plane). It may be utilized to predict nanoparticle formulation stability over time. It was determined using a DLS approach (Zetasizer, Marvelon, UK),[14] the sample was diluted with deionized water and analyzed.

Determination of Drug Entrapment Efficiency

The drug was centrifuged for 10 minutes after it was newly formulated. The supernatant layer was collected and filtered using a 0.45 micropore filter. Using a UV-visible spectrophotometer, the quantity of unincorporated drug was determined at 225 nm (dilution may be required). Using the equations below, the entrapment efficiency and loading efficiency. Quantity of free drug in the supernatant was subtracted from the original amount of drug taken. The experiment was performed three times for each formulation, the average value was taken.[15]

$$\textbf{Entrapment effeciecy} = \frac{Total\ drug - Free\ drug}{Total\ drug} x100$$

$$\textbf{Loading efficiency} = \frac{Total\ drug - Free\ drug}{Total\ lipid} x100$$

In-vitro Release Profile

The dialysis bag diffusion method was utilized to study drug release for 8 hours, using phosphate-buffered solution (pH 7.4) as the release medium. For the optimized formulas with the lowest particle size, the RNB release profile from the RNB-NLC was assessed. In a summary, a prescribed volume containing 10 mg of RNB was loaded in a dialysis bag (cellulose membrane with molecular weight cut-off (8000-14000)), clamped, and submerged in a glass vial containing 250 mL of release medium at 37 ± 0.5°C, then swirled at 50 rpm using a magnetic stirrer. A 1-mL sample was taken at specified intervals of (0, 0.5, 1, 2, 3, 4, 5, 6, and 8 hours). The release medium was replaced with the same amount of fresh milieu to ensure sink conditions. After that, the collected samples were passed through a 0.45 m syringe filter, and the quantity of RNB was determined using a UV visible spectrometer with a detection wavelength of 225 nm. The data were presented as the mean of three replicates (n = 3). The cumulative amount of rizatriptan benzoate released over time was determined.[16]

Fourier Transform Infrared Spectroscopy (FTIR)

The FTIR spectrum of RNB, GMS, and physical mixture of the optimum formula was recorded using an FTIR spectrometer (Shimadzu, Japan) in a spectral region between 4000 and 400 cm^{-1} and analyzed by transmittance technique. Compatibility studies were carried out at room temperature by FTIR to investigate any interactions may happen in the formulation.[17]

Differential Scanning Calorimetry (DSC) Analysis

The DSC was used to investigate the thermograms of pure RNB, GMS, and a physical combination of these substances. A 2 mg sample was weighed, sealed in an aluminum pan, and then placed in a DSC instrument. The sample was heated to a maximum temperature of 300°C at a rate of 10°C per minute, with nitrogen serving as a blank gas.[18]

Statistical Analysis

The results of the experiments were presented as the mean of triplicate samples plus standard deviation, and they were analyzed using one-way analysis of variance (ANOVA) to determine whether the changes in the applied factors are statistically significant at the level of ($p < 0.05$) and nonsignificant at the level of ($p > 0.05$).

Table 1: Preparation of RNB Nanostructured Lipid Carrier Formulas

	FR 1	*FR 2*	*FR 3*	*FR 4*	*FR 5*	*FR 6*
Rizatriptan benzoate (mg)	10	10	10	10	10	10
Glyceryl monostearate (mg)	37	34	37	34	---	---
Bess wax (mg)	-----	----	----	---	37	34
Oleic acid (mg)	3	6			3	6
Castor oil (mg)	----	---	3	6	---	---
Tween 80 (w/w)	3	3	3	3	3	3
Lecithin (w/w)	1.5	1.5	1.5	1.5	1.5	1.5
Deionized water up to (mL)	2	2	2	2	2	2
Rate of Homogenization r.p.m x (100)	200	200	200	200	200	200
Time of Homogenization (min.)	20	20	20	20	20	20

RESULT AND DISCUSSION

Screening of Lipids

Starting with stage one of formulation creation, a logical, sensible, and wise strategy will always provide a good and consistent outcome. The initial step in the production of NLC, considered the most sophisticated point of lipid-based formulations, was the screening of major components, including solid and liquid lipids. However, relatively little work has been documented on preliminary component screening for NLC design. Usually, in the case of conventional lipid-based formulation, solid and liquid lipids are selected based on the solubility of the targeted drug in a specified lipid.[19]

Solid Lipid Solubility of RNB

The solubility survey was applied to several types of solid lipid. It was eventually found that rizatriptan benzoate has a high solubility in GMS compared to other types, so it will be used as a basic kind in preparing RNB loaded NLC, Figure 2(a) shows this finding. To prevent crystallization and getting high loading and encapsulation efficiency, the mixture of RNB and lipids had been agitated at temperatures above 10°C at its melting points. The final visual assessment was known as a very clear, transparent lipid–drug mixture, the absence of targeted crystals in each lipid refers to the maximum solubilization.

The solubilization phenomenon was based on structural and physicochemical properties of a particular drug which cannot be generalized for every hydrophilic drug candidate, the solubility findings could be justified based on structural interaction (formation of hydrogen bond) which might be taking place between solid lipids and drugs leading to the formation of a stable complex. Different characters associated with GMS were shared to eliminate its solubilization property. The hydrophilicity character is due to the two hydroxyl groups, lack of high esterification state, and no unsaturated bonds. In addition to the above-noticed benefits, a proper lipid matrix selection will offer an improvement in physical and chemical stability (e.g., oxidation, hydrolysis, and photosensitive) of the entrapped drugs.[20]

Screening of Liquid Lipids

Accordingly, data obtained from solubility studies of RNB in various liquid lipids were depicted in Figure (2b). Compared to semi-synthetic and hydrogenated vegetable oils, it was found that rizatriptan benzoate has low solubility in oils from natural sources. This could be related to the unmodified edible oils, which are the most biocompatible oil vehicles but are unlucky, they are unable to dissolve a significant quantity of hydrophilic drugs and had low self–emulsification efficiency, whereas semi-synthetic and hydrolyzed vegetable oils were extremely successful in these areas.[21]

Concerning the solubility of RNB in natural vegetable oil, castor oil, and peppermint oil have the highest potency to solubilize the drug molecule, this may be related to the hydrophilicity of castor and peppermint oil, which is due to the presence of hydroxyl groups in the main composition of these oils. Meanwhile, rizatriptan benzoate has the lowest solubility in the soya bean and aloe oil, since these oils have the tendency of hydrophobicity characteristics due to the existence of long-chain unsaturated hydrocarbon.[22]

Oleic acid is classified as a monounsaturated omega–9 fatty acid, long-chain triglyceride. Oleic acid exhibits significantly higher RNB solubility ($p < 0.05$) since it possesses the best solubilization capacity than other oils and this is maybe related to the formation of hydrogen bonding between the carboxylic group of the fatty acids and the drug molecules.[23] Therefore, it was chosen as the best liquid lipid for formulating an RNB-loaded NLC.

Particle Size Analysis

The most important part in the formation of nanoparticles was lipids. As it is known, the lipid part consists of solid lipid and liquid lipid in different proportions. This ratio has different effects on the properties of the prepared NLC according to earlier research. Formulas (FR1 and FR2) are fabricated to investigate the change in the NLC parameter upon alteration in the GMC: Oleic acid ratio.

Because the two lipids, GMS, and oleic acid, are spatially distinct, mixing them causes defects and tortuosity in the crystal order of the lipids, resulting in an increase in the distance between fatty acid chains in the matrix structure of GMS. As a result, the arrangement has a variety of abnormalities.[24]

The results showed that the quantity of liquid lipid plays a significant role ($p < 0.05$) in reducing particle size of NLC since it led to a reduction in viscosity and surface tension thereby producing NLC with smaller size, high surface area.[25]

When the solid lipid and liquid oil ratio was as low as possible, the smallest particle size could be obtained. Prior literature reported that the enhancing ratio of the liquid oil will lead to small particle size since an increment in the percentage of solid lipid generated particle agglomeration effect leads to increased particle size. Furthermore, the solid lipid content increase has increased emulsification time, which may be related to the melting point enhancement. An increase in the weight ratio of solid lipids led to globules with increased size.[26]

Moreever, it was claimed that adding liquid oil to the lipid matrix reduces the particle size of the NLC which may

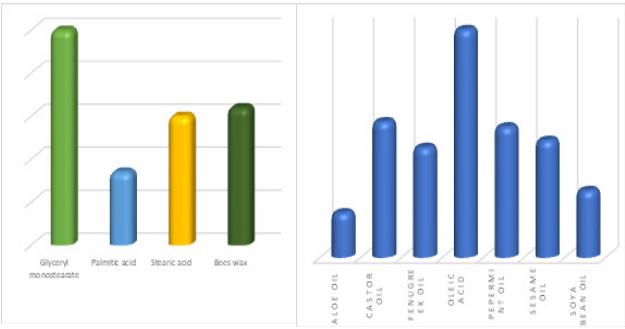

Figure 2: Solubility of rizatriptan benzoate in different types of (a) solid lipid and (b) liquid lipid

be related to the matrix's increased molecular mobility after oil addition, which promotes the creation of tiny particles populations. Hu *et al.* also found that adding liquid oil to a formulation decreases surface tension, resulting in smaller particles owing to reduced viscosity within the NLC.[27]

It is interesting to note that other researchers discovered the opposite of what was seen in this study, that an increase in solid lipid leads to a decrease in particle size. As an instance, Sangsen *et al.* found that the particle size of the prepared NLCs significantly decreases with increasing solid and decreasing liquid lipid content of the nanocarriers, *i.e.,* the particle size decreases with increasing solid lipid: liquid lipid ratio at a constant total lipid phase content (Figure 3).[28]

Since the lipid phase represents the framework of NLC production, formulas (FR3, FR4, FR5, and FR6) are prepared from different types of green solid and liquid lipid, respectively as a trial to convert pharmaceutical production to the safer side. The results of the tests carried out on the prepared samples revealed a significant change ($p < 0.05$) in particle size and polydispersity index. The exact reason behind these outcomes may not be well understood but many hypotheses can postulate certain causes. The first one is related to chemical nature and the degree of crystallinity between these lipids type and the drug used.[29]

Another explanation highlights the variability of the melting point of the lipids used, since its effect on the viscosity of the lipid phase and thus on the energy required to break the emulsion particle to a smaller one, beeswax has a high melting point as compared to GMS and this means more power was needed to destruct such particle so large particle size can be predicted, a similar result was obtained by Sharifi *et al.*[30]

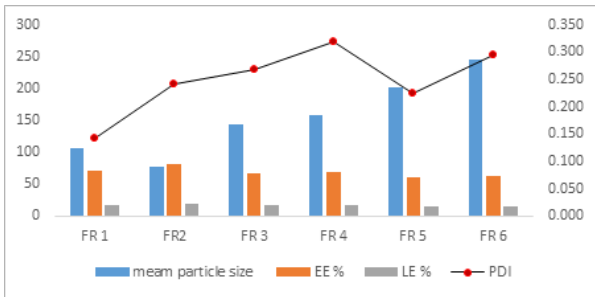

Figure 3: Effect of type and concentration of solid and liquid lipid on the particle size, Entrapment efficiency percent, Loading Efficiency percent of RNB -NLC (FR1-FR6).

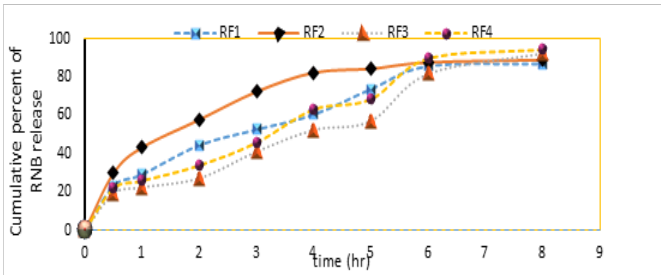

Figure 4: Release profile of RNB – NLC in phosphate buffer solution (pH (7.4)) (FR1-FR4).

Entrapment Efficiency and Loading Capacity

The amount of drug incorporated in the prepared NLC represent an obstacle especially for hydrophilic drug, so the entrapment efficiency and drug loading capacity of RNB-NLC (FR1, FR2, FR3, FR4, FR5, and FR6) were investigated, the obtained outcomes revealed an enhancement in both values upon increasing the percentage of oleic acid from 7.5 w/w to 15 w/w as shown in Figure 4, It might be due to the incorporation of liquid lipids which could lead to massive crystal order disturbance, and the resulting matrix of lipid particles had great imperfections in the crystal lattice and leaves enough space to accommodate drug molecules, thus, leading to improved drug loading capacity and drug entrapment efficiency. From another point of view, higher entrapment efficiency in a formulation containing oleic acid is related to the higher solubility of the rizatriptan benzoate in liquid lipid as compared to solid lipid in selected drug/lipid ratio.[31]

Moreover, the degree of crystallinity of solid lipid has a direct effect on the void space available to accommodate drug molecules, the addition of liquid lipid leads to enhancing deformity of solid lipid crystal if the liquid lipid makes a high degree of deformation culminates in tiny particle size, a minuscule polydispersity index, and a significant quantity of the drug being captured in the matrix.[32] Also, when the oleic was replaced by castor oil, the entrapment efficiency and loading efficiency decreased since the drug has more solubility in oleic acid. Furthermore, it may be related to the increased in particle size associated with castor oil so the total surface area was diminished and consequently, the total amount of drug loaded in the NLC was reduced.

Zeta Potential

Zeta potential reflects the charge on the surface of the prepared RNB-NLC which was related to the component of nanostructured lipid carrier, the value of zeta potential shows a valuable enhancement upon increasing the ratio of oleic acid (data not mentioned) and this may be related to the participation of the negative charge of the hydroxyl group of the oleic acid. Furthermore, changing the oleic acid to the castor oil showed an increment in the zeta potential, it was hypothesized to the more negative charge present on the surface of the castor oil.

In-vitro Release Profile

The basic condition for the success of each pharmaceutical formulation is the drug released from it in a streamlined manner that aligns with the goals to be achieved. The test was carried out on four samples that have the smallest particle size (FR1, FR2, FR3, and FR4). It was performed using phosphate buffer solution pH 7.4 for 8 hours using the dialysis bag method, the release profile obtained was seen in Figure 4.

A predominant biphasic release modern was seen clearly through the investigation of the release pattern of RNB from all the prepared NLC formulas. An early burst of drug release of a high amount is followed by a period of drug release that lasts for a long time. This style of release behavior may be a possible explained assuming the drug-enriched shell of

the RNB incorporation model, which involved a significant amount of the drug being entrapped in the outermost shell of the particle during lipid solidification, the larger surface area associated with the small particle permit efficient contact with dissolution media resulting in an extremely short RNB diffusion pathway, as well as the high stabilizer concentration used in the formulation, which may have increased the amount of drug released into the dissolution medium.[33]

The existence of liquid oil in the backbone of the NLC may facilitate the escaping tendency of the hydrophilic molecules through the imperfect structure and the tortuosity channel in the lipid matrix. Also, as the liquid lipid increased, the imperfection in the crystal structure of glyceryl monostearate was enhanced and at the same time, the diffusion channel may become more distributed.[34] A slow-release model was observed in which the drug incorporated within the lipid template was liberated either through diffusion or after erosion of the lipid particle.[35]

Nevertheless, shape, size, drug hydrophilic solubility and diffusivity in dissolution media, polymorphism status of lipid nanocarriers, pH of the medium, drug loading, and porosity, are different variables that may influence drug molecule release from the nanocarriers. Rizatriptan benzoate has realistic rules for all formulas because of its valuable water solubility and its tendency to escape from the lipid nanoparticles. At all events, the slow release of rizatriptan from developed nanocarriers is not indicative of the undesirability of these nanocarriers for bioactive delivery, because, as mentioned before these nanocarriers have a small size (below 200 nm) and therefore they can be suitable for intranasal transport.[36]

Fourier Transform Infrared Spectroscopy (FIRT)

The FTIR spectroscopic analysis is useful in establishing the compatibility of medicine with other excipients, which is a crucial rule in the selection of the best one. Additionally, the FTIR analysis is a good tool for investigating any structural changes that may occur in the drug due to exposure to severe and demanding circumstances throughout the formulation process.

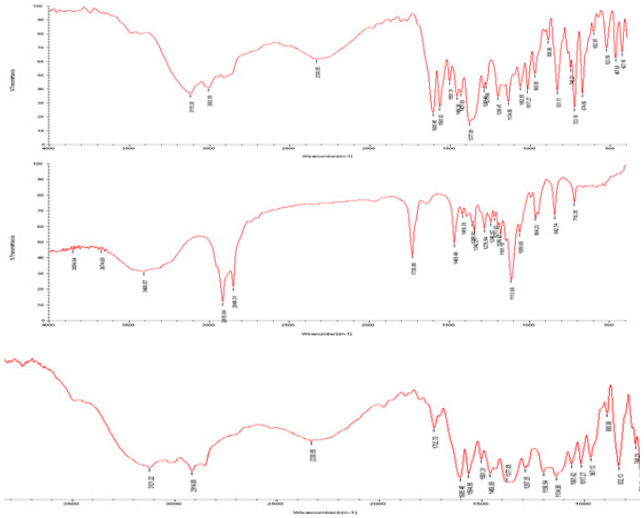

Figure 5: FTIR spectrum of (a) pure rizatriptan benzoate, (b) glyceryl monostearate and (c) physical mixture of FR2 formula.

FTIR of pure RNB, GMS, and physical mixture of the optimized formula (FR 2) were illustrated in Figures 5(a-c), respectively. The FTIR of rizatriptan benzoate show characteristic peaks are 3130 cm^{-1} for N-H stretching, 2939, 2858 cm^{-1} for CH_3, CH_2 stretching, 1604, 1505 cm^{-1} for C=C, C=N stretching, 1454, 1377 cm^{-1} for CH_2, CH_3 bending, NH bend at 1280 and 887, 825, 756 cm^{-1} for CH and C-N stretch at 1134 cm^{-1}, CN out of plane bend, similar results were obtained by Girotra *et al.*[37]

The IR spectrum of GMS exhibited peaks at three positions are 3113.3, 2915, and 2848.5 cm^{-1}. These peaks are due to (C-H) stretching of alkane and the carboxyl group (C=O) stretching peak is observed at 1728 cm^{-1}.

Fortunately, when the accurate investigation of, the major peaks of the drug to be formulated are present, and this categorically guarantees that the chemical integrity and molecular structure of RNB do not tamper throughout the preparation procedure.

DSC

DSC enables the quantitative detection of all processes in which energy is required or produced (i.e., endothermic and exothermic phase transformations). DSC is an effective tool for investigating the melting behavior and crystalline state of nanocarriers and raw materials. Since crystallinity significantly impacts some properties of lipid nanoparticles such as drug loading, drug release, and stability of drugs during storage, studying it can be useful for judgment about nanocarriers features.[38]

The DSC study of the thermal behavior of RNB, GMS, and physical mixture of the same formula component (FR2) were represented in Figures 6(a-c), respectively.

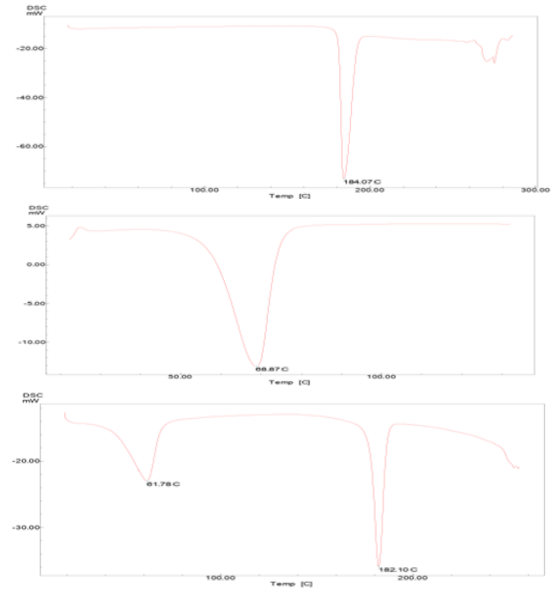

Figure 6: DSC thermogram of (a) rizatriptan benzoate, (b) glyceryl monostearate and (c) physical mixture of the optimized formula FR2.

The drug thermogram shows a sharp endothermic peak at 184.4ºC corresponding to its melting point, indicating RNB purity and the degree of the anhydrous crystalline structure. There is an endothermic peak at 68.87ºC in the DSC thermogram of GMS and the molecular organization is a very well-organized crystalline structure.

DSC thermograms of the physical mixture (Figure 6c) revealed that there is no considerable change observed in the melting peak of rizatriptan benzoate pure drug (184°C) and drug with GMS which indicates that no interaction takes place during the formulation. Moreover, it confirms the decrement of the ordered and crystalline structure of the RNB and the presence of the polymorphic

CONCLUSION

Depending on the present project's findings, successful rizatriptan benzoate-loaded NLCs were obtained utilizing different lipid species and ratios (solid and liquid lipid). The high shear homogenization technique can be regarded as a suitable method for formulating rizatriptan benzoate-loaded NLC with suitable particle size and entrapment efficiency. Also, changing the type of solid and liquid lipid along with their ratio could be employed to achieve the desired outcome. The drug was released from the selected formula (FR2) in a biphasic pattern. While the drug and other formula additives were found to be compatible in FTIR and DSC investigations.

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