

Research Article**Encapsulation of Ketoprofen loaded lipid microspheres: Preparation, characterization and release kinetics**Vikrant K. Nikam^{1*}, Sanjay Jain², Guru Mohanta³¹Amrutvahini College of Pharmacy, Sangamner 422 608, (MS), India²Institute of Pharmacy, Bundelkhand University, Jhansi 284128 (U.P.) India³Department of Pharmacy, Annamalai University, Annamalai Nagar 608 002, (TN), India

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Abstract

Objective: A melt solidification technique has been developed to obtain controlled-release lipid microspheres of Ketoprofen. The objective of the present study was to minimise the unwanted side effects of Ketoprofen drug by kinetic control of drug release by entrapping Ketoprofen into gastro resistant, biodegradable waxes such as beeswax, Ceresin Wax microspheres using congeable emulsified dispersion technique utilizing a wetting agent. Solid, discrete, reproducible free flowing microspheres were obtained. **Material and Methods:** The Ketoprofen loaded lipid microspheres were prepared using modified melt solidification technique. The drug loaded in microspheres was found to be stable and compatible with waxes as confirmed by DSC and FTIR methods. **Results and Conclusion:** The yield of the microspheres was up to 93.0%. Microspheres had smooth surfaces, with free flowing and good packing properties. It indicates that the obtained angle of repose, % Carr's index and tapped density values were well within the limit. More than 95.0% of the isolated spherical microspheres were in the particle size range of 310-320 μm as confirmed by scanning electron microscopy photographs. The technique and the lipid microspheres were evaluated on the basis of process and desired yield, size distribution, crushing strength, and drug release. The release of drug was controlled for more than 12h. The release kinetics followed different transport mechanisms. The drug release performance was greatly affected by the materials used in microsphere preparations, which allows absorption in the intestinal tract.

Keywords: Ketoprofen, bees wax microsphere, ceresin wax microsphere, controlled release

Introduction

Dosage forms that can precisely control the release rates of drug have made an enormous impact in the formulation and development of novel drug delivery systems. Recently, scientists are occurring on development of dosage form at nano and micro level. Microsphere is one of such dosage form (Bodmeier et al., 1992). The most significant features of microspheres are microscopic size and more surface area. Through selection of optimum method and polymer we can explore the use of microsphere for variety of beneficial functions (Schaefer et al., 1990). Ketoprofen is a novel a non-steroidal anti-inflammatory drug used to treat rheumatoid arthritis, osteoarthritis analgesic,

antipyretic and mild to moderate pain (Nadia et al., 2002). It inhibits cyclooxygenase-1 and -2 (COX-1 and COX-2) enzymes reversibly, which decreases production of pro inflammatory prostaglandin precursors (Gokonda et al., 1994). The starting dose of ketoprofen is a single dose of 50mg produce general analgesic. The usual maximum dose should be 200mg. It is practically insoluble in water, having only 40% oral bioavailability (Kim and Ulrich, 2003). Ketoprofen undergoes extensive first pass metabolism. The dosage of ketoprofen varies depending upon the reason for its use. When used to treat analgesia, 25–100 mg is the typical starting dosage. During treating rheumatoid arthritis, a total daily dosage of 50–150 mg is usually effective and 200 mg per day may be needed for maximum effect (Frazier et al., 2001). Considering the long regimen of osteoarthritis and rheumatoid arthritis, the administration of ketoprofen was reported to induce adverse side (Reich, 1999; Angary et al., 1998; Giannola et al., 1995). Side effects that occur in more than 5% of patients taking

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ketoprofen include stomach ulcer, bleeding, ringing in the ear and visual disturbances skin rash, nausea, vomiting, diarrhea, mouth ulcer, headache, dizziness and drowsiness. To achieve maximum therapeutic effect with a low risk of adverse effects, controlled released preparations are preferred (Chauhan et al., 2005). The side effects could be lowered by controlling the drug release and by adjusting the absorption rate. This can be achieved by employing suitable modifications in the manufacturing process (Benita and Zouai, 2006). Delivering the drug in the intestine from lipid microspheres could be manipulated by suitable melt solidification techniques (Fieldman and Newton, 2002). The chief characteristics of melt solidification technique are their impermeability to gastric juices but susceptibility to intestinal juices (Kojima and Nakagami, 2002), waxes are biocompatible, non-immunogenic material used for the entrapment of drug, used for controlling drug release in the intestinal tract (Pardhakar et al., 2002). The objectives of the present study are to formulate, characterize and study the in vitro drug release from wax/lipids microspheres loaded with Ketoprofen. The pattern of drug release from the Ketoprofen microspheres compared with two lipids by using different ratios of drug and wax.

Materials and methods

Materials

Ketoprofen was kindly supplied by Themis Laboratories, Mumbai (India). All other reagents and chemicals used were of analytical grade.

Preparation of Wax Microspheres

Weighed amount of ceresin wax were melted separately in china dish using water baths. Drug previously passed through sieve no.100 was dispersed in the melted wax mass and stirred to obtain a homogeneous melt. These individual mixtures were poured into 200 ml of mixture of dispersant medium containing 100ml of pH 7.4 Phosphate buffer solution (to minimize the solubility of drug) and 100ml of PVA (1%), which was previously heated to a temperature higher than melting point of wax ($>+5^{\circ}$). Tween 80 (2% w/w) was added to the mixture containing waxes. The whole mixture was mechanically stirred at 900 rpm using a stirrer (RQ-127D). Spherical particles are produced due to dispersion of molten wax in the aqueous medium. The mixture was stirred continuously at 900 rpm at a higher temperature ($>+5^{\circ}$) of the melting point of waxes/fat for 3 min. The temperature of the mixture in the beakers was cooled rapidly to 4°C by the addition of cold water. The resultant solid spheres collected by filtration were extensively washed with water to remove any drug and surfactant residues. Air drying was carried out at room temperature for 48hr produced discrete, free flowing solid microspheres. Similarly above process was carried out with Bees wax by melted in china dish at a temperature of 75°C . Total 6 formulations were prepared by

Table 1. Formulation table for Ketoprofen Microspheres by melt solidification technique

| Formulation Code | Quantity of Lipids | | Drug(gm) |
|------------------|--------------------|---------------|----------|
| | Ceresin Wax gm) | Bees Wax (gm) | |
| K1 | 9 | - | 3 |
| K2 | 12 | - | 3 |
| K3 | 15 | - | 3 |
| K4 | - | 9 | 3 |
| K5 | - | 12 | 3 |
| K6 | - | 15 | 3 |

varying concentration of both lipids as shown in table 1.

Size analysis of microspheres

The separations of the microspheres in to various size fractions were carried out by sieve analysis technique and SEM analyzed the size of microspheres.

Micromeritic properties

Tap density of the prepared microspheres was determined using tap density tester and % Carr's index was calculated. Angle of repose was assessed to know the flowability of wax microspheres.

Scanning electron microscopic studies and sphericity determination

SEM photographs were taken using scanning electron microscope JEOL 5400, Tokyo, Japan, at suitable magnification at room temperature. The photographs were observed for morphological characteristics and to confirm spherical nature of the microspheres. To determine the sphericity, the tracings of lipids microspheres (magnification 45 X) were taken on a black paper using Camera Lucida, (Model-Prism type, Rolex, India) and circulatory factor was calculated (16). The sphericity of microspheres was calculated using the equation, $S = \frac{p^2}{12.56 \times A}$, where A is area (cm^2) and p is perimeter (cm)¹.

Differential scanning calorimetry (DSC)

DSC studies were carried out on Netzsch thermal analyzer with 200F DSC module. Calorimetric measurements were made with the help of an empty cell as the reference. The instrument was calibrated using high purity indium metal as standard. The dynamic scans were taken in nitrogen atmosphere at the heating rate of $10^{\circ}\text{C}/\text{min}$. The sample wash thermetically sealed in an aluminum crucible. Nitrogen gas was purged at rate of 10 ml/min. for maintaining inert atmosphere.

Fourier transform infrared spectroscopy (FTIR)

FTIR spectra of pure drug, empty microspheres and drug

loaded microspheres were obtained using KBr pellet method (applying 600 kg/cm²). The drug excipient interactions were measured by powder diffuse reflectance on a FTIR spectrophotometer (Shimadzu, Model 8033, USA) in the wave number region 400-4000 cm⁻¹.

X-ray diffractometry (XRD)

The crystalline nature of drug is performed by XRD analysis technique. The X-Ray Diffraction pattern of Pure drugs Ketoprofen, and drug loaded lipid microsphere were recorded using (Phillips Xpert pro, Germany) X ray diffractometer with a Cu-tube (k(alpha) 1.541, 45 kV, 40 mA), at a scanning speed of 0.30°C/min and the peaks were indexed in Bruker (Germany).

Loose surface crystal study

This study was conducted to estimate the amount of drug present on the surface of the pellets. 100 mg of pellets was suspended in 100 ml of phosphate buffer (pH 7.4). The samples were shaken vigorously for 15 min in a mechanical shaker. The amount of drug leached out from the surface was analyzed spectrophotometrically at 259 nm. Percentage of drug released with respect to entrapped drug in the sample was recorded.

Estimation of drug loading

Drug incorporated lipid microspheres of each batch was selected and powdered in a mortar. 100 mg of drug loaded lipid microspheres was accurately weighed and added in to 100 mL volumetric flask. To this, 100 mL dichloromethane was added. This solution was stirred for 60 min, till the entire drug leached out. The solution was filtered and 1 mL was withdrawn from this solution and added in to 10 mL volumetric flask and volume was made to 10 mL (10 µg/mL) with phosphate buffer pH 6.8. Drug content was estimated UV spectrophotometrically at 259 nm.

In vitro studies

USP XX1 dissolution apparatus type II was employed to study percentage of drug release from various formulations prepared. Accurately weighed quantities of drug (Ketoprofen 50 mg) loaded microspheres of each batch were taken in 900 ml dissolution medium (2 hr in pH 1.2 hydrochloric acid buffer and 3hr upto 24hr in pH 7.4 phosphate buffer) and stirred at 100 rpm by maintaining at a temperature of 37°C ± 0.5. At prefixed time intervals 1ml of sample was withdrawn and filtered through 0.4 µm membrane filter. Then the withdrawn is diluted to 10ml. The volume of the dissolution medium was adjusted to 900ml at every sampling time by replace same 1ml of dissolution medium in order to maintain the sink condition. Then the samples were analyzed Spectrophotometrically at 259 nm and thereby the cumulative percentage drug release was obtained from the following formulae.

Amount of drug present = Concentration × Dilution factor × Conversion factor × Amount of stock solution.

Cumulative % drug release = Amount of drug present / Amount of drug to be present

Results and discussions

Evidence have shown in the recent years that lipid materials have the physical properties and behavior suitable to prepare gastro resistant, biocompatible, biodegradable microspheres to release the entrapped drug in the intestinal lumen.

In the present study, a modified novel congeable dispersion emulsified cooling induced solidification method was employed using inert lipids and non-toxic solvents to entrap the drug. In the present study, various parameters were studied such as drug and wax ratio, stirring speed and time, concentration of emulsifier added, volume of the aqueous phase used, effect of pH on drug entrapment, temperature of the aqueous phase and rapid cooling studies. Therefore the influence of the above parameters was highlighted. When the pH value of the external aqueous phase was highly alkaline, the solubility of the drug was reduced and the encapsulated amount of the drug increased. The maximum drug load was obtained at pH 7.4. When pH value changes from 7.4 to 5.0, the percent of drug loading reduced from 12.78 to 3.0%, 13.95 to 2.7 for bees wax and ceresin wax formulations respectively.

In the present study, it was found that 200 ml of aqueous phase or dispersant medium suitable for producing the spherical microspheres. Resultant microspheres did not have any surface irregularities and are non aggregated. As the volume of external phase increased, the yield was reduced and the resultant microspheres were irregularly shaped. When the volume of the aqueous phase was less than 150 ml, the resultant microspheres were highly aggregated in nature and highly impossible to distinguish as individual microspheres. In order to avoid the formation of irregularly shaped larger particles, in the present method, 200 ml of aqueous phase containing 100ml of pH 7.4 Phosphate buffer solution (to minimize the solubility of drug) and 100ml of PVA (1%) was used.

Incorporation of Ketoprofen into bees wax, ceresin wax microspheres required the addition of tween 80 as a surfactant or emulsifier, at an optimum concentration to reduce the interfacial tension between the hydrophobic material and external aqueous phase. An attempt was made to incorporate drug in the wax microspheres without the addition of a surfactant. But the process failed, as it resulted in an aggregate cake like mass during the solidification of wax. This may be due to repulsion resulting from high interfacial tension between the hydrophobic waxy material and external aqueous phase. It was found that tween 80 having a HLB value of 15 was suitable to increase

substantially dispersion of waxy material in external aqueous phase and promote drug incorporation in the wax microspheres. To obtain an optimal surfactant concentration, various concentrations ranging from 1.0 to 2.0% (w/w) of the total formulation were tested. Discrete microspheres with good flow properties using an optimum concentration of surfactant 2 % w/w (tween 80) were used. Concentrations of tween 80 ranging from 1.0 to 1.9 % w/w failed to produce reproducible microspheres. The resultant lipids microspheres were composed of irregular masses, which were not possible to distinguish as individual microspheres. A similar emulsifier concentration was reported for wax microspheres prepared by meltable dispersion method (Gowda and Shivakumar, 2007).

Temperature of the aqueous phase was maintained at 5°C higher than the melting point of the lipids in the corresponding formulations. From SEM studies it was observed that the resultant microspheres were free from surface irregularities, except some wrinkles. It was also observed that when the temperature of the aqueous phase was less than the 5 °C than the melting point, a big waxes flakes were produced.

In the present study, to produce the spherical discrete microspheres, an optimum drug to lipids phase ratio of 1:5 w/w was used. It was found that higher the amount of drug to wax ratio (2:5) produces aggregate masses during the cooling process. It may be due to reduced melting point of the lipids materials. SEM photographs also indicated the presence of the crystals on the surface of the microspheres. The resultant microspheres were unsuitable for pharmaceutical uses. Hence an optimum 1:5 ratio was used to prepare microspheres.

Sieve analysis data obtained for prepared lipid microspheres were in the size range of 106 to 500 µm and 55.43 to 74.18 % were of size fraction 250µm. It was observed that the average size of the microspheres ranged between 310 to 320 µm. The important factor that influences the size distribution of microspheres is the optimum stirring speed and stirring time.

A stirring speed of 900 rpm and stirring time of 3 min was used to obtain reproducible microspheres. It was observed that with the increase in the stirring speed from 900 to 1200 rpm there was a decrease in the average size of the spheres and recovery yield of the microspheres, due to small sized microspheres, which were lost during successive washings. When the stirring speed was lower than 900 rpm, larger pellets were a formed. It was also found that an increase in stirring time, from 4 to 8 min (at a stirring speed of 900 rpm), there was a decrease in the recovery yield of microspheres. When the stirring time lower than 3 min, melted waxes/fat materials adhered to the sides of the beaker during the cooling process, resulted in lower recovery of yield.

Micro particulate drug delivery systems are formulated as single unit dosage forms in the form of capsule or tablet. Such microparticulate systems should possess the better and adequate micromeritic properties (Gowda et al., 2007). The obtained micromeritic properties are given in table 2.

The values of angle of repose were well within the range, indicating reasonable good flow potential for the microspheres. The tapped density values ranged between 0.97 g/cm³ to 1.47g/cm³. The results of % compressibility index ranges from 10.24 % to 14.67 %, suggests good flow characteristics of the microspheres table 2. The better flow property indicates reasonable and good flow potential of prepared microspheres.

SEM photographs showed that the lipid microspheres were spherical in nature, had a smooth surface with inward dents and shrinkage, which is due to the collapse of the wall of the microspheres figure 1 photograph reveal the absence of crystals of the drug on the surface of microsphere, indicating uniform distribution of the drug within the microspheres. The rate of solvent removal from the microspheres exerts an influence on the morphology of the final product (Adeyeye and Price, 1994).

Table 2. Micromeritic properties of the drug loaded lipid microspheres

| Formulation | % Yield (%w/w) | Mean particle size (microns) | Angle of repose | Tap Density | Compressibility Index |
|-------------|----------------|------------------------------|-----------------|-------------|-----------------------|
| K1 | 83.92 | 56.60 | 22.10 | 0.98 | 11.48 |
| K2 | 86.91 | 41.13 | 26.37 | 1.24 | 12.86 |
| K3 | 88.08 | 39.22 | 28.06 | 1.47 | 14.67 |
| K4 | 88.13 | 68.22 | 26.82 | 0.97 | 10.24 |
| K5 | 89.32 | 44.50 | 25.97 | 1.24 | 12.33 |
| K6 | 92.45 | 29.25 | 25.48 | 1.45 | 13.07 |

Table 3. Drug loading properties of wax microspheres

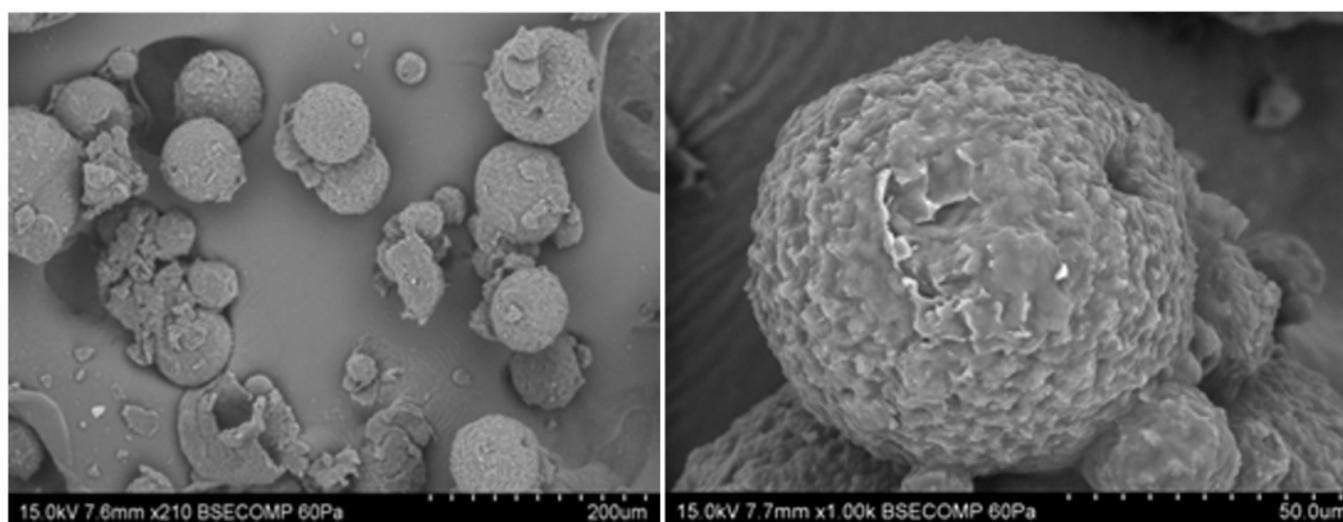
| Formulation | Drug entrapment (%) | Drug Content (mg) |
|-------------|---------------------|-------------------|
| K1 | 42±0.34 | 10.64 |
| K2 | 55±0.27 | 11.13 |
| K3 | 64±0.73 | 10.73 |
| K4 | 49±0.37 | 12.43 |
| K5 | 64±0.15 | 12.88 |
| K6 | 77±0.33 | 12.83 |

Table 4. In-vitro Release Kinetics of Ketoprofen Prepared Microspheres

| Formulation code | Mathematical models (release kinetics) | | | | |
|------------------|--|----------------------|----------------|----------------|----------|
| | Zero order kinetics | First order kinetics | Higuchi's | Peppas's | n |
| | r ² | r ² | r ² | r ² | |
| K1 | 0.795808 | 0.850889 | 0.929998 | 0.961708 | 0.803121 |
| K2 | 0.805889 | 0.89637 | 0.929894 | 0.964494 | 0.819335 |
| K3 | 0.816571 | 0.903098 | 0.928949 | 0.962812 | 0.853261 |
| K4 | 0.998109 | 0.892385 | 0.924367 | 0.958215 | 0.876955 |
| K5 | 0.99826 | 0.910485 | 0.927146 | 0.962712 | 0.88036 |
| K6 | 0.996027 | 0.916066 | 0.925271 | 0.962917 | 0.885622 |

DSC studies were performed on pure drug and drug-loaded lipid microspheres have shown sharp endothermic peaks. Ketoprofen exhibits a sharp endothermic peak at 95.86°C presented in figure 2. The two polymers Bees wax and ceresin wax showed endothermic peak at 58.78°C and 61.4°C which corresponds to melting process. It was observed that presence of the endothermic peak of the drug at 58.87(K6) in the drug loaded lipid microspheres indicates, that the drug is uniformly

distributed in the microspheres and drug has not shown any interaction with different polymers used in preparing the different formulations. The peak intensity corresponding to the melting of ketoprofen decreased in the thermograms of ketoprofen loaded lipid microspheres. These results indicate that only a small fraction of the drug substance existed in the crystalline state. The presence of melting endotherm was in the ketoprofen loaded lipid microspheres, which indicates

**Figure 1.** SEM photomicrographs of loaded microspheres (K6)

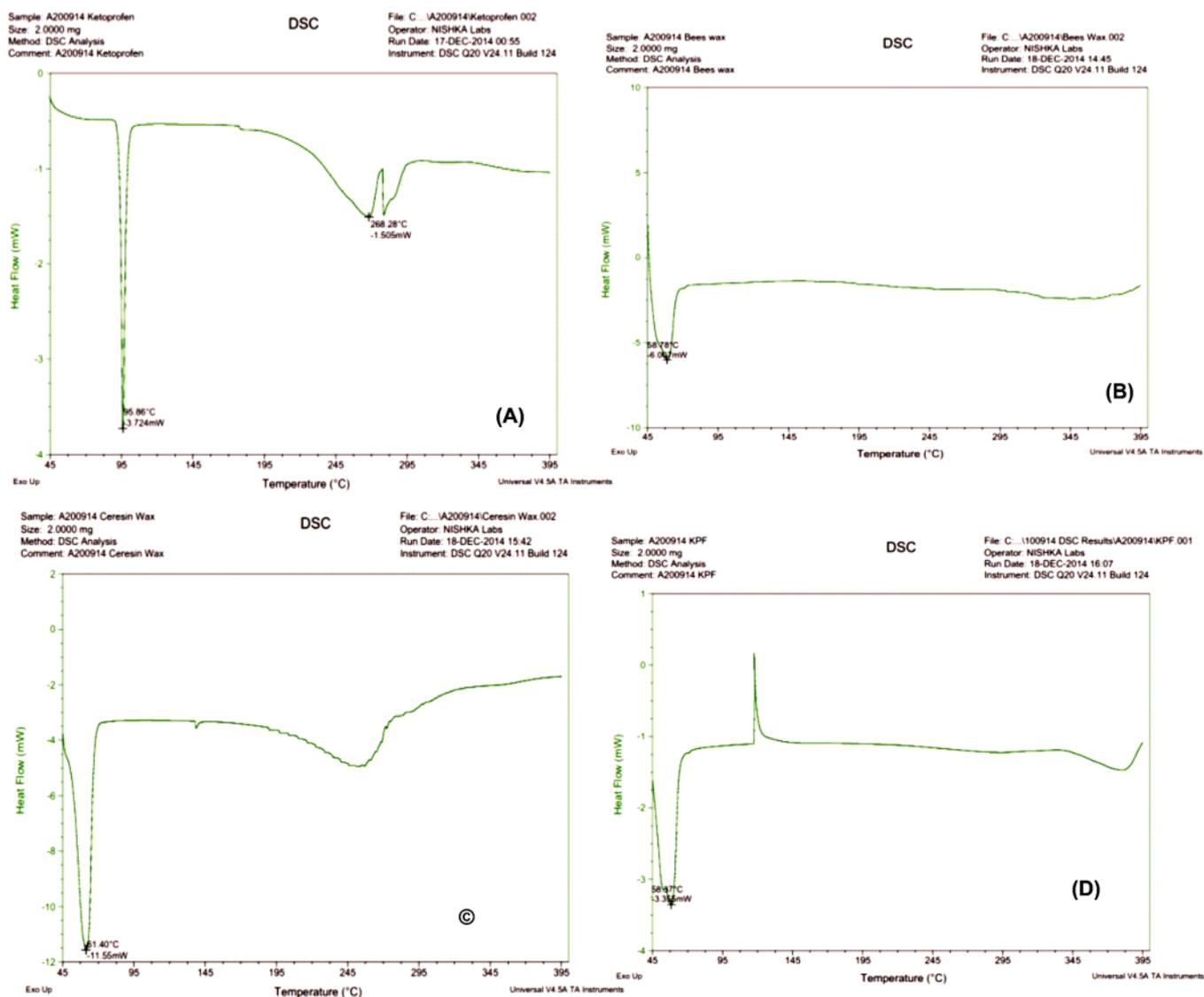


Figure 2. DSC Curve of Ketoprofen (A), Bees wax (B), ceresine wax (C), Formulation K6 (D)

that ketoprofen was completely dispersed inside the wax microspheres.

From the FTIR studies, the characteristic bands for important functional group of pure drug ketoprofen, empty microspheres and drug-loaded lipid microspheres were identified. It was observed that 2983-2930 cm^{-1} (Aromatic C-H stretch carboxylic acid O-H stretch), 1695-1649 cm^{-1} (C=O stretch), 1580.8 cm^{-1} (Aromatic C=C stretch), 1455.8 cm^{-1} (CH-CH₃ deformation), 2904 cm^{-1} ((C-H) stretch plus O-H deformation), 1687.2 cm^{-1} (Carboxylic O-H out of plane deformation), 860-640 cm^{-1} (C-H out of plane deformation for substituted aromatic) presented in Figure 3. FTIR spectra showed that the characteristics bands of ketoprofen were not altered after successful encapsulation without any change in their position, indicating no chemical interactions between the drug and lipid used. Hence the FTIR spectrum shows the same characteristic peaks when it is formulated into Microspheres.

XRD pattern of pure ketoprofen showed principal peak at 22.60° and intense peaks at 11.48°, 13.23°, 14.46°, 16.28°, 16.98°, 17.37°, 19.22°, 20.10°, 21.72°, 22.60°, 23.99°, 26.11°, 27.22°, 28.48°, 29.51°, 30.43°, 32.58°, 34.5°, 36.22°, 38.77°, 39.55° and 42.22°, principal peak at 21.81° & intense peaks at 21.81°, 24.18°, 30.27°, 36.38°, 22.19°, 38.45°, 40.23°, 42.82°, 43.94°, 49.03°, 52.24° to ceresine wax, principal peak at 21.32°, & intense peaks at 19.29°, 21.32°, 23.68°, 29.68°, 35.83°, 40.16°, 43.22° to bees wax, Ketoprofen loaded lipid microspheres (K6) showed principal peak at 21.44° & intense peak at 19.32°, 21.44°, 23.83°, 29.91°, 36.04°, 38.12°, 40.74°, 43.66°, 48.74° to K6 respectively, as presented in Figure 4. It observed that the peaks which are formed in drugs due to crystalline, but the drug when formulated with polymers had not shown these characteristic peaks. X-ray diffraction patterns revealed the crystalline nature of pure ketoprofen X-ray diffractogram

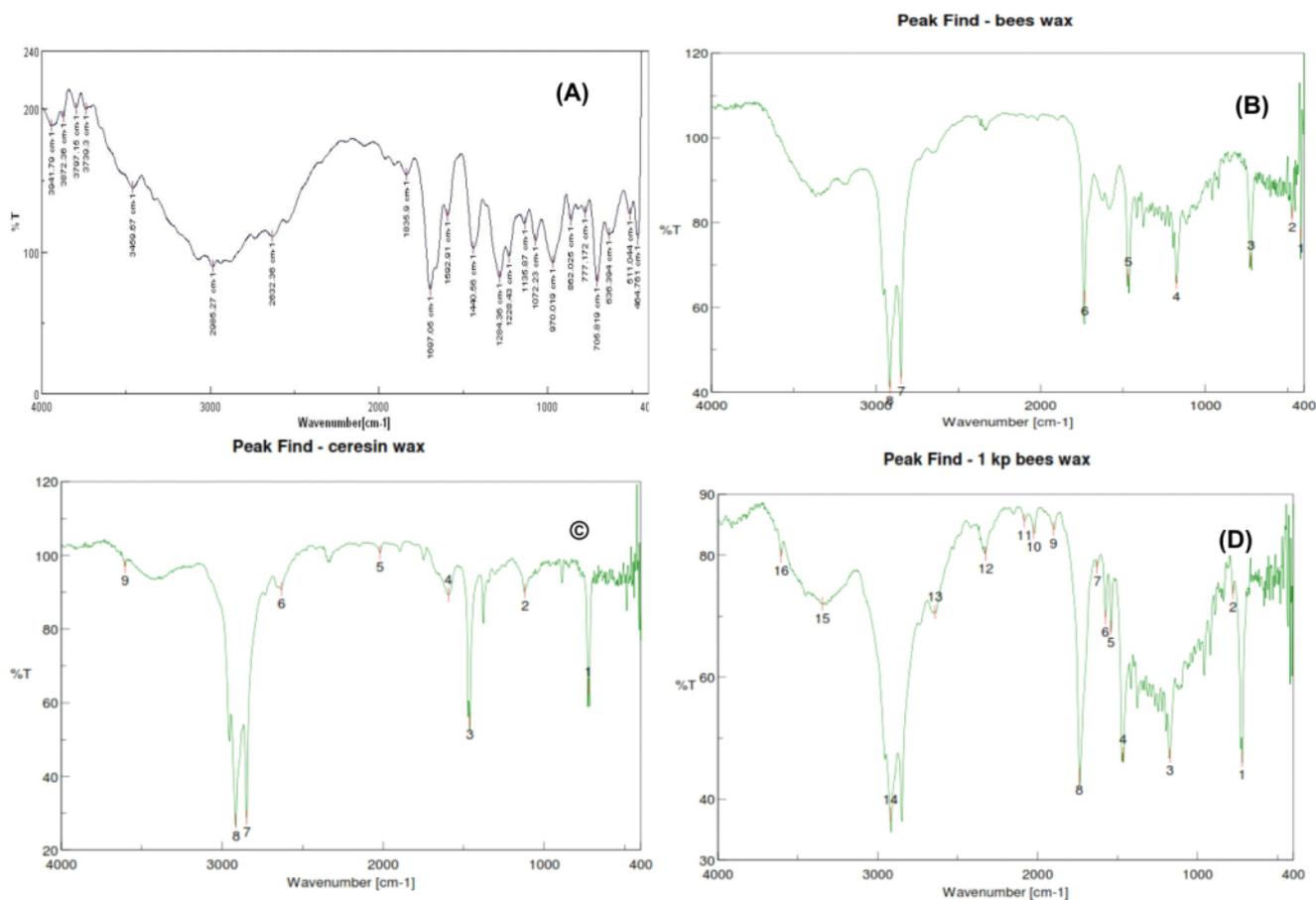


Figure 3. FTIR of Ketoprofen(A), Bees wax(B), ceresine wax(C), Formulation K6(D)

of Ketoprofen showed number of sharp and intense peaks but increased peak width was observed in XRD pattern of ketoprofen loaded lipid microspheres.

Loose surface crystal (LSC) study is an important parameter giving indications of the amount of drug on the surface of the lipid microspheres. Physical state of ketoprofen in all formulations with different drug loading was investigated by polarized light microscopy. Microscopic studies indicated that crystalline ketoprofen was observed clearly in formulation K6 (Drug loading was 12.83 % w/w) than other formulations.

The drug loading and drug encapsulation efficiency of lipid microspheres (K1 to K6) are given in the table 3. Drug content in all the formulations were in the range of 10.64 to 12.88 % w/w. Drug content was least in formulation K1 (10.64 % w/w) and high for formulation K6 (12.88 % w/w). Drug encapsulation efficiency was found to be more in formulation K6 (77%) and less in formulation K1 (42 %). It is only because of different kinds of polymer used for the respective formulations. From the in-vitro release studies it was observed that, no major changes in release of drug at gastric pH from lipid microspheres. At the end of 24hr, in vitro drug release from K1 (83.92%), K2 (86.91 %), K3 (88.08 %), K4 (88.13%), K5 (89.32%), & K6 (92.45 %) in the intestinal environment. Drug was

released in a biphasic manner consisting of initial fast release followed by a slow release in intestinal pH from the lipid microspheres (20). The decreased in vitro drug release from lipid microspheres might be due to more hydrophobicity and influence of molecular weight of lipids. The in vitro drug release was considerably increases from the lipid microspheres when compared with each other in different ratios (Aravindaram et al., 2012).

The rate of drug release followed first order release kinetics and numerical data fitted into Peppas's model showed that, the mechanism of drug release from lipids microspheres was non fickian diffusion. After an initial burst effect, the subsequent release of drug from microspheres was slow, and the influence of molecular weight was observed. The rate of drug release followed first order kinetics and numerical data fitted into Peppas' equation (Maheshwari et al., 2003). All the prepared formulations are having diffusion exponent value (n) more than 0.45 and less than 1, this indicates that the release mechanism follows non-Fickian diffusion.

The linear regression analysis of Ketoprofen Microspheres shown as R² values in table 4. When the data were plotted according to the First-order equation, for all formulations (K1

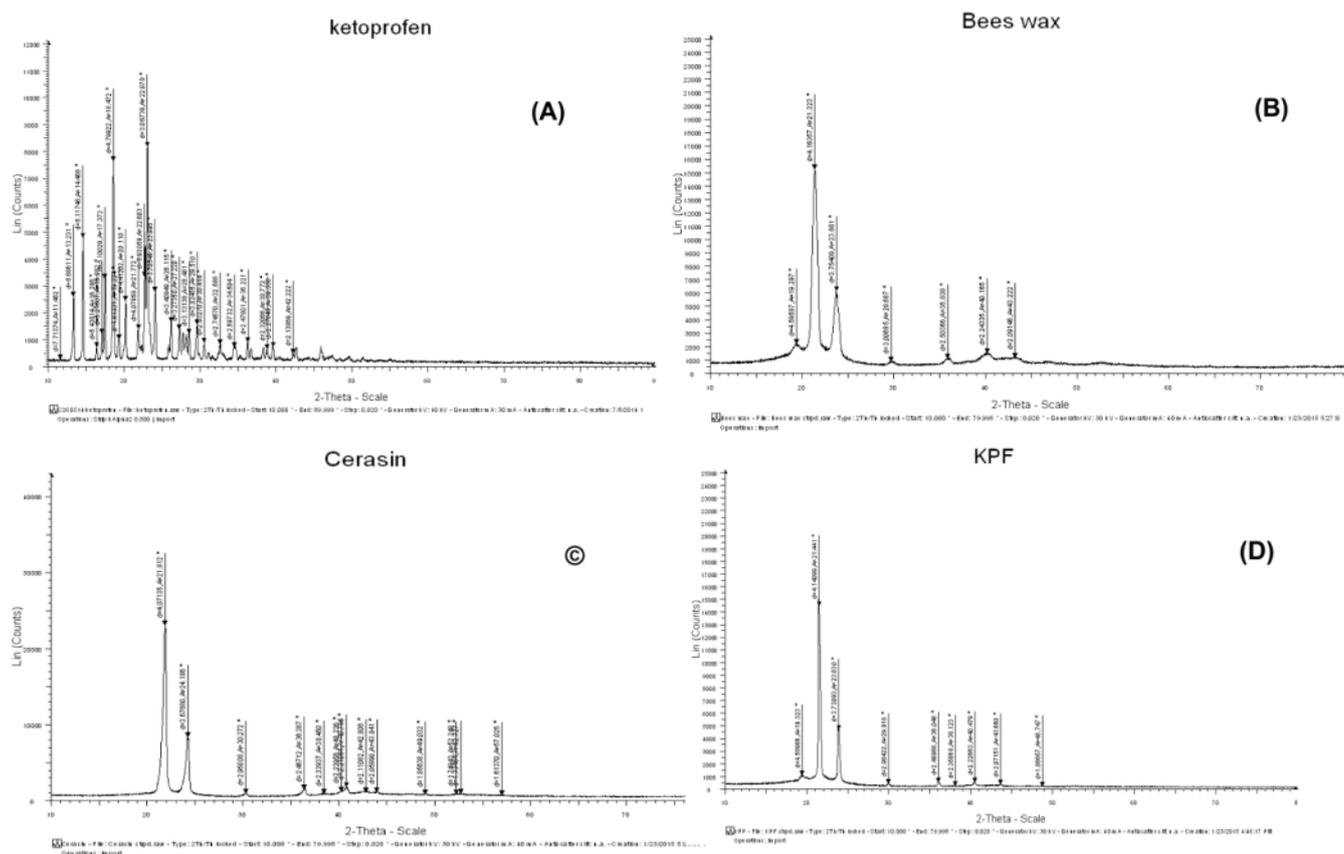


Figure 4. XRD spectrum of Ketoprofen (A), Bees wax(B), ceresine wax(C), Formulation K6(D)

to K6) showed a fairly linear, with regression (R^2) values between (0.851 to 0.916) clearly indicate that the drug wasn't released as per first-order mechanism. All the formulations expressed by Higuchi plots shows linearity with regression coefficient (R^2) value as (0.924 to 0.93) also not close to infinity indicate the drug release process is not as per Higuchi plot. The Zero order plots of all formulations were found to be highly linear, and close to infinity as indicated by their high regression (R^2) values as (0.795 to 0.996). Therefore, it was ascertained that the drug permeation from these formulations could follow either near Zero or Zero order kinetics. Hence the release mechanism was shifted from the first order to Higuchi followed by zero order release kinetics.

In the drug release mechanism the data were fitted to Peppas equation. In the present study also it was observed that n value was obtained between (0.803 to 0.885) for all formulations in Table 4. These values, suggesting that more than one mechanism may be involved in release kinetics. In the case of formulation KPF6 with Bees wax shows non Fickian Diffusion with n value as (0.885).

It observed that the formulations K1 to K3 are containing 1:3, 1:4 and 1:5 ratios of which were prepared by Melt dispersion technique with Ceresin wax as a polymer. The cumulative percentage drug release showed in K1, K2 and K3 was 96.66%, 93.38%, and 91.25% of drug release for 24hrs. The formulations

K4 to K6 are containing 1:3, 1:4 and 1:5 ratios of which were prepared by Melt dispersion technique with bees wax as a polymer. The cumulative percentage drug release showed in K4, K5 and K6 was 94.16%, 90.49% and 87.4% of drug release for 24hrs. It was observed that, formulation K6 shows extended release up to 24 hrs. There is initial burst release followed by constant release. It was observed that the drug release from the formulations decreased with increase in polymer concentration this is because more will be the wax concentration more time is taken to diffuse the drug molecule figure 5.

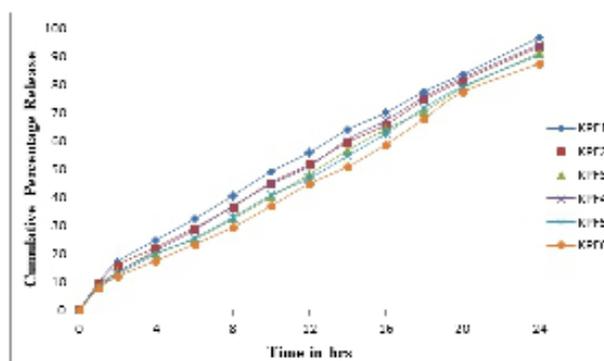


Figure 5. In Vitro Drug release data of Ketoprofen Microspheres (K1-K6)

The formulations K3 and K6 showed the longer duration of drug release for 24hrs in simulated intestinal fluid, in addition to completing retarding the drug release in gastric medium. This is due to the polymer Bees wax. The drug release from waxy microspheres was considerably retarded from the waxes. So that K6 was taken as a best formulation to achieve a prolonged maintenance of effective concentrations of drug.

Conclusion

In the present study to obtain Ketoprofen lipid Microsphere, a drug having a melting point above 100°C. The development of Ketoprofen loaded reproducible lipid microspheres could be prepared for intestinal release of Ketoprofen using congeable dispersion emulsified method without affecting the chemical nature of the drug. The lipids obtained by this simple, rapid, economical, does not imply the use of toxic organic solvents and one-step processing technique have shown controlled drug release up to 24 hours. The Ketoprofen lipid microspheres were spherical with smooth surface and good micromeritic properties. The drug release profile was significantly affected by the properties of lipids used in the preparation of microspheres.

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Conflicts of interest: Not declared.

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