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# DESIGN OF SUSTAINED RELEASE PELLETS OF OFLOXACIN USING HOT MELT COATING TECHNIQUE

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**Abstract:**
*The intention of research was to design and development of sustained release multi- component drug delivery system using hot melt coating technique. Hot melt coating technique was used initially to formulate sustained release drug delivery system of ofloxacin and finally to formulate sustained release multi- component drug delivery system of rifampicin plus isoniazid and metoprolol tartrate plus hydrochlorothiazide respectively. Ofloxacin pellets were prepared by rotary shaker pelletizer and hot melt coated with different coating levels of various ratios of stearic acid: palmitic acid. Ofloxacin hot melt coated pellets were spherical with smooth surface and also complies parametric standards for hardness, friability and drug content. Ofloxacin pellets were found stable during stability study. In vitro dissolution study of ofloxacin pellets demonstrated that drug dissolution was reliant upon the physicochemical properties of the drug and more specifically on drug's aqueous solubility, coating compositions and coating levels. Aceclofenac pellets were hot melt coated using cow ghee and ethyl cellulose. Hot melt coated aceclofenac pellets showed good flow property and pass the tests like friability, hardness and drug content. Aceclofenac pellets release profile demonstrated more than 65% release in 4 hours. Since the method used for hot melt coating did not facilitate more than 10% of coating composition, further retardation of aceclofenac release could not be achieved. Stability study showed no major change in physicochemical characteristic and dissolution.*

**Key Words**: *Ofloxacin, Pellets, Physicochemical, friability, hardness, flow property*

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## INTRODUCTION:

Ofloxacin preparations commercially available are conventional and taken twice a day to achieve therapeutic effects. Therefore, purpose of this research is to prepare sustained release ofloxacin pellets using hot melt coating technique. Stearic acid and palmitic acid are used as hot melt coating agents.

**Preparation of ofloxacin pellets:** Ofloxacin and excipients were passed through a 120 mesh and transferred to the glass bowl. Formulation of ofloxacin pellets was shown in table 3.4. All ingredients were geometrically mixed thoroughly and 5% w/v PVP K-30 solution was used as binder and this coherent mass was screened from sixteen sieve to form an extrude. Then extrude was transferred to rotatory shake pelletizer and operated for 15 min at 200 rpm. The drug pellets dried at 60°C in tray dryer 3 hours. The 16/20 mesh pellets were selected for HMC (Jaiswal SB., 1995). Microcrystalline cellulose and PVP K-30 solution were used as bulk former and binder respectively. Since ofloxacin shows pH dependent solubility, citric acid was used to maintain acidic microenvironment in the pellets (Cui Y. et. al., 2008).

**Table-1: Formulation of ofloxacin pellets**

| Sr. No. | Ingredient | Amount (mg) |
|---|---|---|
| 1. | Ofloxacin | 200 |
| 2. | Microcrystalline cellulose (Avicel PH 101) | 4 |
| 3. | Citric acid | 5 |
| 4. | PVP K-30 solution | Q.S. |

**Hot melt coating to ofloxacin pellets:**16/20 Ofloxacin pellets were hot melt coated with different coating compositions as shown in table 2.

**Table-2: Formulation of hot-melt coating composition**

| Formulation | Stearic acid: Palmitic acid (w/w) | PEG 1450 (%) | Coating level (%) |
|---|---|---|---|
| B1 | 1:5 | 10 | 7.5 |
| B2 | 1: 7.5 | 10 | 7.5 |
| B3 | 1:10 | 10 | 7.5 |
| B4 | 1: 7.5 | 10 | 3 |
| B5 | 1: 7.5 | 10 | 5 |
| B6 | 1: 7.5 | 10 | 10 |

Stearic acid and palmitic acid were weighed accurately and melted with continuous stirring. PEG 1450 was added about 10% w/w of coating composition on dry basis into the molten mass with continuous mixing. Pellets were hot melt coated at 55-60 degree Celsius by adding slowly as shown in table 3.. After coating, the pellets kept for 24 hr at 25°C (Sakarkar DM. et. al., 2009).

**Table-3: Coating parameters for HMC of ofloxacin pellets**

| Sr. No. | Process parameters | Settings |
|---|---|---|
| 1. | Pellet charge | 500 g |
| 2. | Pellet size | 16 /20 mesh |
| 3. | Pan speed | 25 rpm |
| 4. | Pellet bed temperature | 60°C |
| 5. | Relative humidity | 30-50% |
| 6. | Processing time | 30 min |
| 7. | Curing conditions | 30°C for 24 hr |

**Molding the pellets in unit dose:** Ofloxacin 200 mg pellets were packed in '0' size hard gelatin shell.

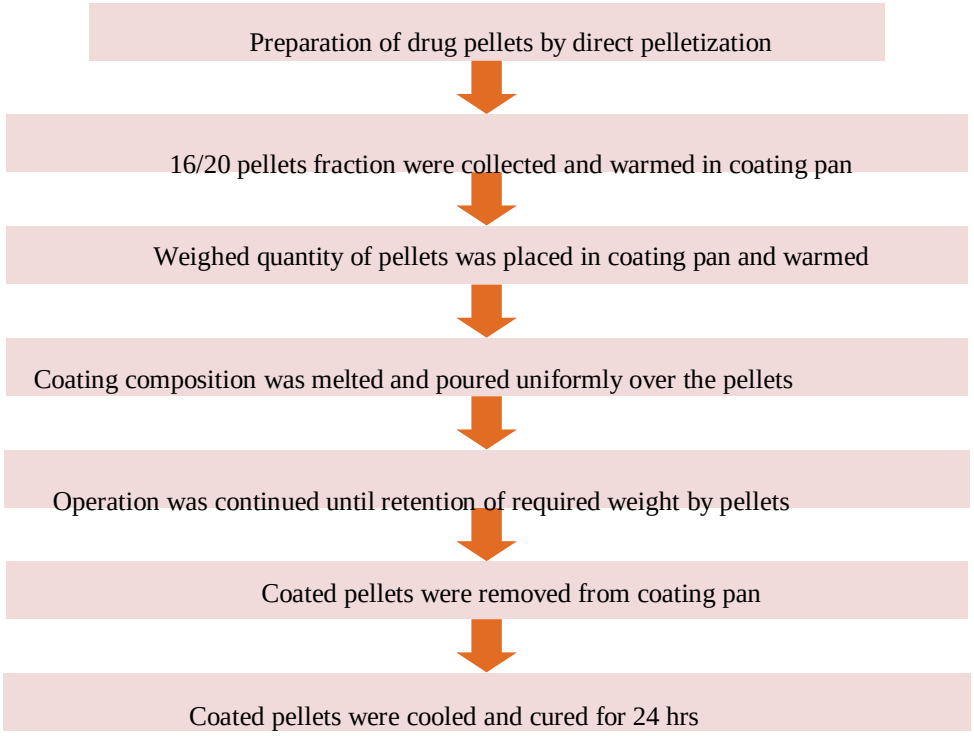



**Figure-1: Schematic representation of preparation of HMC pellets of ofloxacin.**

**Evaluation of pellets:**
The uncoated and coated pellets were evaluated for physical and micromeretic properties as per procedure described (Fekete R. et. al., 1998, Gandhi R., et. al., 1999).

**Drug content:**
Accurately weighed 500 mg of pellets were grind in the mortar. Ofloxacin 50 mg and 30 mL of methanol was taken in 100 mL volumetric flask, sonicated for 15 min and level adjusted to 100 mL with 0.1N HCl. Then assay was performed spectrophotometrically at 293 nm. Drug content was determined in triplicate for each sample using following equation (United States Pharmacopoeia, 2002) –

$$\% \text{ Drug content} = \frac{\text{Absorbance of test}}{\text{Absorbance of standard}} \text{ X } 100$$

***In vitro* dissolution study:**

**Release of ofloxacin from uncoated pellets in different media:**
It was performed in 0.1N HCl, pH 4.5 PB and 7.4 PB. Pellets equivalent amount to 200 mg ofloxacin was packed in '0' size hard gelatin shell, drug release was performed at 50 rpm using basket and samples were analyzed spectrophotometerically at 293 nm.

**Dissolution of market sample of ofloxacin:**
Ofloxacin dissolution from modified release marketed formulation (Zanocin OD, Ranbaxy Labs, India) was used as innovators product. Pellets of ofloxacin were coated in such a way that to achieve the release profile similar to modified release marketed formulation.

**Dissolution of prepared formulations:**
Ofloxacin dissolution was performed to evaluate the modified release characteristics imparted by HMC using basket apparatus, six station dissolution assembly. Dissolution conditions used for the study are indicated in table 3.7. Modified release pellets were studied for dissolution following above said conditions. Aliquots of filtered dissolution samples were analyzed

spectrophotometrically at 293 nm (Mathur SC. et. al., 1992).

**Table-3: *In vitro* dissolution conditions for ofloxacin hot-melt coated pellets**

| Sr. No. | Parameters | Specifications |
|---|---|---|
| 1. | Dissolution test apparatus | USP Type I (Basket type) |
| 2. | Paddle speed | 50 rpm |
| 3. | Quantity of pellets | Equivalent to 200 mg of ofloxacin |
| 4. | Temperature | 37 ± 0.5°C |
| 5. | Time | 12 hr |
| 6. | Dissolution medium | 0.1N HCl |
| 7. | Volume of dissolution medium | 900 ml |
| 8. | Sampling time | 0.5, 1, 2, 4, 6, 8, 10 and 12 hr |

**Ofloxacin HMC formulations dissolution study:**
Dissolution was carried out using USP basket type apparatus with 0.1N HCl and PB pH 4.5 and PB 7.4 respectively. Ofloxacin 200mg was transferred in a basket and operated the dissolution apparatus for 50 rpmat900 mL. Finally samples were analyzed spectrophotometrically at 293 nm (Cui Y. et. al., 2008).

**Effect of osmotic pressure on ofloxacin release:**
Dissolution was carried out using basket apparatus with 0.1N HCl with 0%, 0.9%, 2.0% and 5.0% NaCl individually. Ofloxacin 200mg was transferred in a basket and operated the dissolution apparatus for 50 rpmat900 mL. Finally samples were analyzed spectrophotometrically at 293 nm (Cui Y. et. al., 2008).

**Kinetic data analysis:**
Ofloxacin release data was fixed into Higuchi, Hixon- Crowell & Korsmeyer-Peppas models. From regression coefficient ($R^2$) values of respective formulation, best fitted model for each formulation was selected (Costa P. et. al., 2001, Moore JW. et. al., 1996).

**Selection of optimized formulation:**
Ofloxacin pellets were compared for dissolution study with marketed modified release formulation (Zanocin OD, Ranbaxy Labs, India) and based on the results of *f*1 and *f*2 values ofloxacin formulations were selected (FDA, Guidance for dissolution testing of IR & Development, Evaluation and application of *in vitro/in vivo* correlations for ER solid oral dosage forms, 1997).

**Effect of storage temperature on drug release from coated pellets:**
Effect of the storage temperature was studied to assure the robustness of pellets, whether the storage temperature affects the prepared formulations or not. Storing the optimized formulation at 25°C, 37°C and refrigerated temperature (2- 8°C). The effect was studied by *f*1 and *f*2calculations.

**Preparation of two more batches to confirm reproducibility:**
Optimized formulation were prepared two more times to confirm whether the optimized formulation shows reproducible result or not. Ofloxacin release of these batches were performed under same conditions and their release profiles were compared with optimized formulation profile using f1 and f2 calculations.

**Stability studies of pellets:**
Formulation B2 coated pellets 200 mg of ofloxacin were packed into hard gelatin capsule shell and transferred in amber colored bottles wrapped in aluminum foil. Then bottles were stored at temperature 40°C/75% RH for 6 months. Ofloxacin hot melt coated pellets were studied for assay, dissolution and physical appearance for 2, 4 & 6 months. Results were evaluated for 0 time and RT (Elizabeth B. et. al., 2000, Kanvinde SA. et. al.,

## ANALYSIS OF OFLOXACIN:

**Organoleptic characteristics of ofloxacin:** Table

4 shows colour, odour and taste of ofloxacin as per description terminology.

**Table-4 Organoleptic characteristics of ofloxacin**

| Sr. No. | Characteristic | Result |
|---|---|---|
| 1. | Description | Crystalline |
| 2. | Colour | Off white |
| 3. | Odour | Faint acetous |
| 4. | Taste | Slightly bitter |

**Melting point:** MP of ofloxacin observed from 250 – 255 degree celsius.

**FT-IR spectrum of ofloxacin:**

The FT-IR spectrum was used to confirm the purity of drug by comparing the sample drug spectrum with the standard spectrum of ofloxacin. The spectrum shows following functional groups at respective frequencies. Ofloxacin IR spectrum was carried out in potassium bromide pellet for wave number range of 2000 to 650 $cm^{-1}$. The principal peaks were observed at wave number 1459,1621,1715,1086 $cm^{-1}$ and were represented in figure 1.

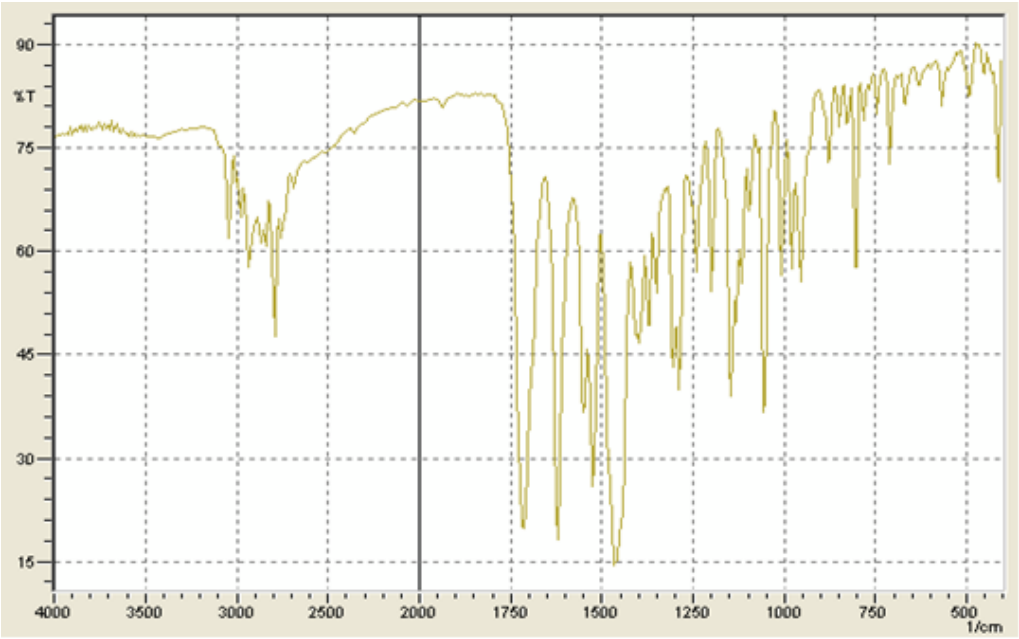



**Figure-2: IR Spectra of ofloxacin.**

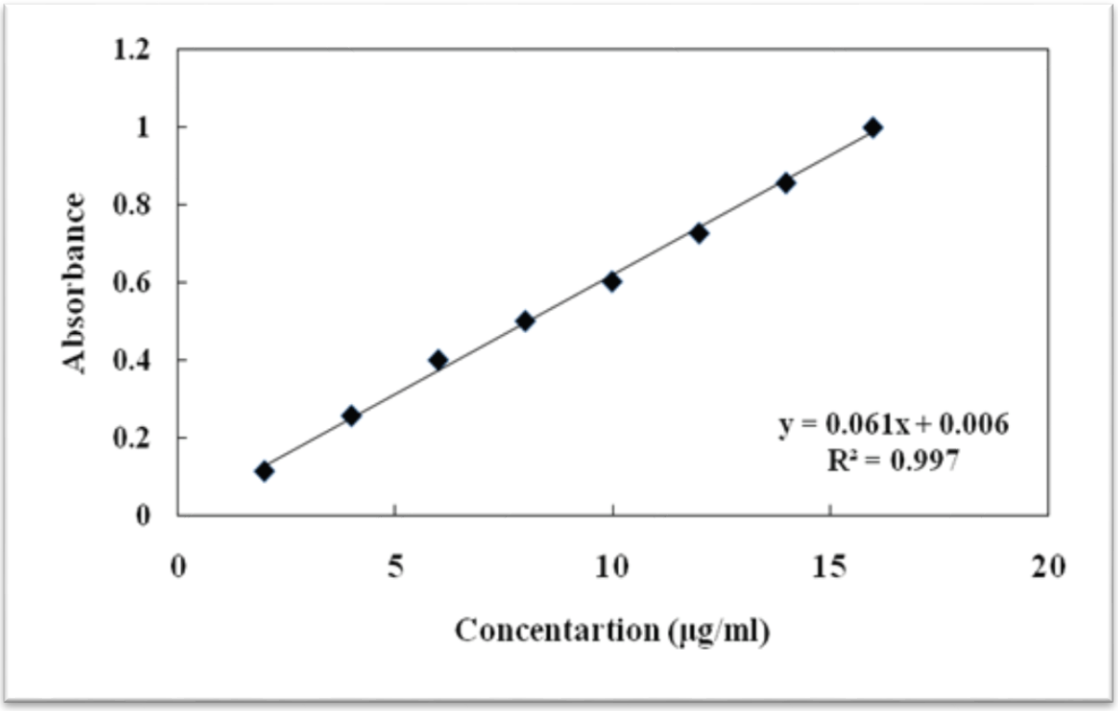



**Figure-3: Standard graph of ofloxacin in 0.1N hydrochloric acid.**

**Standard graphs of ofloxacin:** The standard graphs of ofloxacin in 0.1N hydrochloric acid, PB (pH 4.5, 6.8 and 7.4) and distilled water were plotted shows good linearity with $R^2$ values 0.997, 0.998, 0.998, 0.998 and 0.998 respectively.

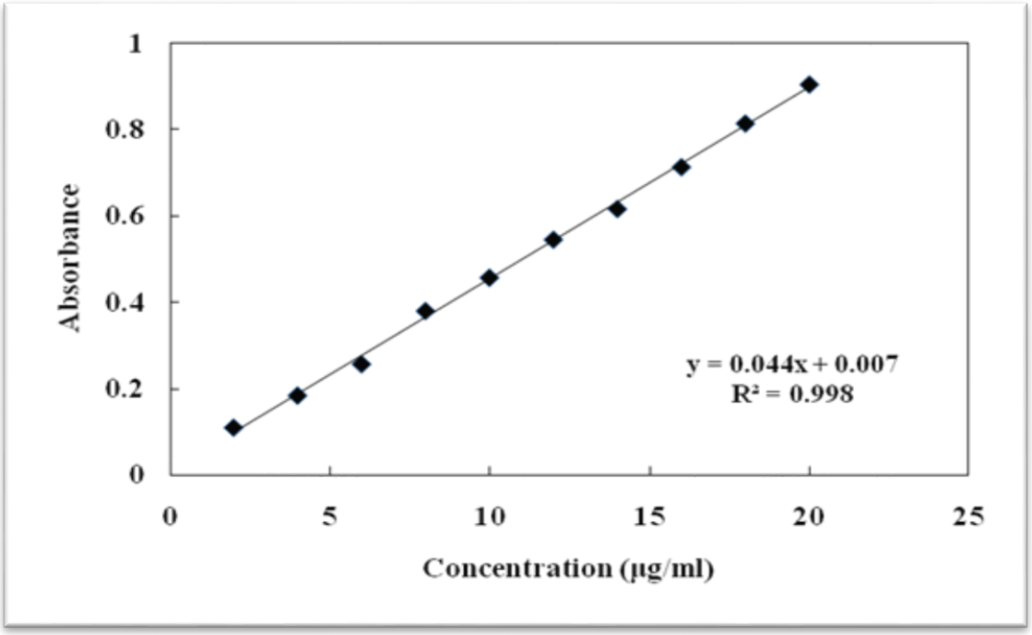



**Figure-4: Standard graph of ofloxacin in PB pH 4.5**

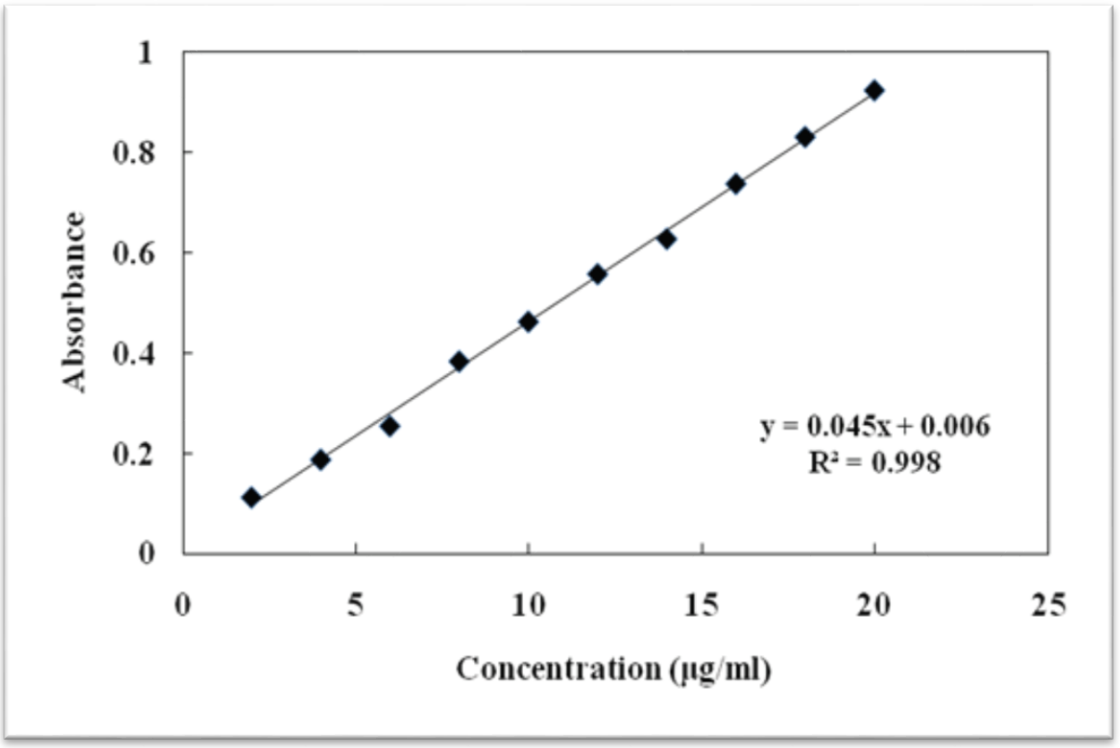



**Figure-5: Standard graph of ofloxacin in PB pH 6.8.**

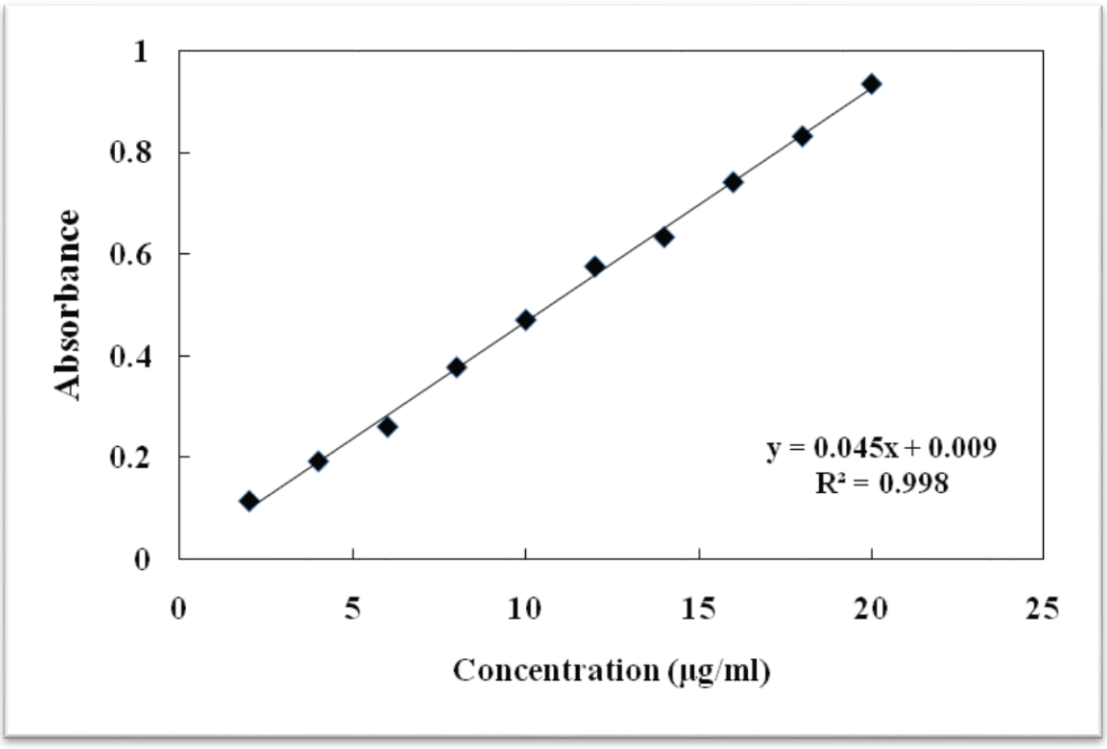



**Figure-6: Standard graph of ofloxacin in PB pH 7.4.**

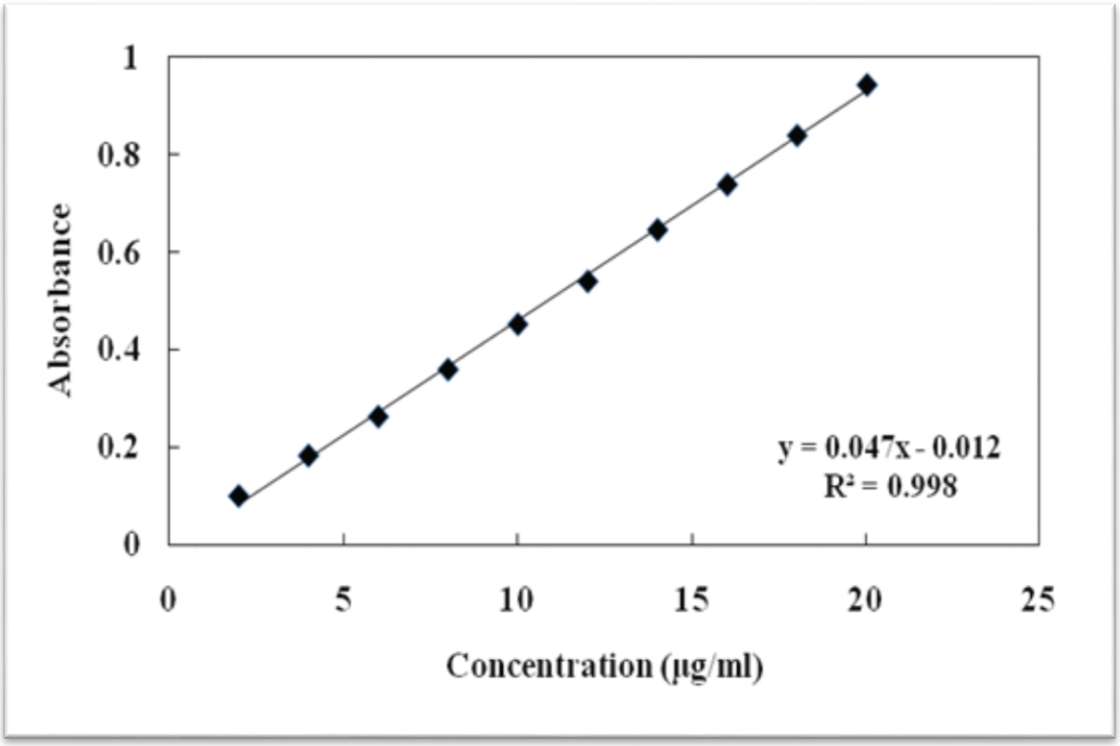



**Figure-7: Standard graph of ofloxacin in distilled water**

**Solubility analysis:** Ofloxacin was observed as slightly soluble in water and PB (pH 4.5, 6.8 and 7.4), and soluble in 0.1 N HCl. Ofloxacin has shown pH dependent solubility. Figure 8 shows that ofloxacin solubility decreases with increase in pH of medium.

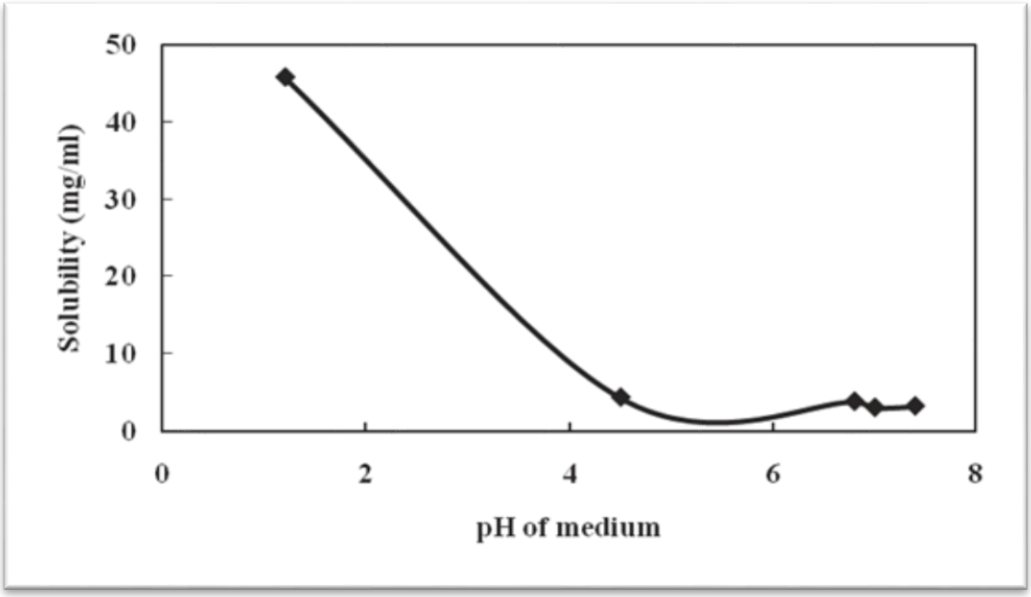



**Figure-8: Ofloxacin solubility at room temperature in various pH medium**

**Partition coefficient:**
Partition coefficient of ofloxacin was 0.154 in 1- octanol/water system & 0.105 in 1-octanol/phosphate buffer pH 7.4.

**Analysis of SA and PA:**
Both SA and PA comply the specifications as per given in USP NF shown in table 5.

**Table-5: Analysis of stearic acid and palmitic acid**

| Sr. No. | Parameters | Stearic acid | | Palmitic acid | |
|---|---|---|---|---|---|
| | | Limits | Result | Limits | Result |
| 1. | Iodine value* | ≤ 1.5 | 1.43 ± 0.001 | ≤ 1.5 | 1.48 ± 0.002 |
| 2. | Acid value* | 195-200 | 198 ± 1.241 | 217-220 | 217 ± 1.142 |
| 3. | Saponification value* | 197-200 | 198 ± 1.312 | 208-222 | 218 ± 1.561 |
| 4. | Melting point (°C) | 68-70 | 65-70 | 59-63 | 60-65 |
| 5. | Refractive index* | 1.4-1.6 | 1.430 ± 0.002 | 1.4-1.6 | 1.427 ± 0.003 |
| *Indicates values in (Mean ± S.D.) when samples were evaluated in triplicate. | | | | | |

**Preparation of ofloxacin modified release pellets:** Figure 4.7 shows that ofloxacin solubility was more in acidic medium compared to basic. Therefore, it was necessary to regulate ofloxacin release in acid media (Zhang XR. et. al., 2005). Palmitic acid was frequently employed for ER. More than pH 5.0-5.5 reduces the capacity of drug to retard drug release and the dissolution of stearic acid at a pH higher than 5.5 is almost in dependent of its amount (Patil AT. et. al., 2012). The prepared formulations were dominated by palmitic acid and stearic acid. Stearic acid, Palmitic acid and polyethylene glycol 1450 make the pellets porous when released in water. Hence, the concentration of PEG 1450 used was very much critical.

## CHARACTERIZATION OF UNCOATED PELLETS AND HMC PELLETS:

**Photomicrography:**
SEMs of ofloxacin pellets shows the uniformity of coating and smoothness surface of pellets before and after coating shown in figure 9.

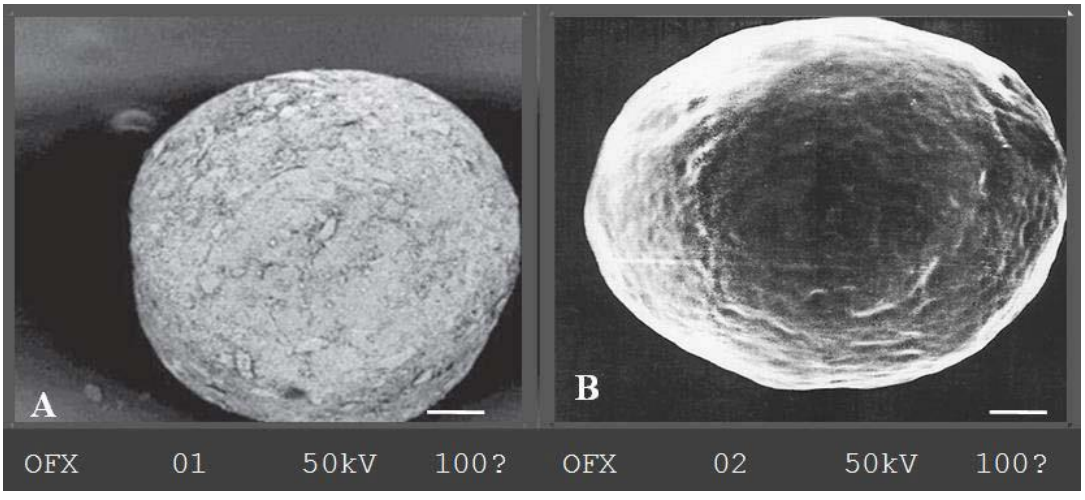



**Figure-9: SEMs of ofloxacin (A) uncoated and (B-) hot melt coated pellets (50X).**

**Mean pellet size: F i g 9** show the mean pellet size of coated and uncoated ofloxacin pellets. The mean size of uncoated pellet of ofloxacin was found to be 864µ and for coated pellets mean pellet size was ranging from 874 to 890µ.

**Angle of repose (θ):** Angle of repose value of uncoated ofloxacin pellets was found to be 35.70°. Hot melt coated ofloxacin pellets values were 17.75° to 29.15°. Table 4.3 shows the values of all the formulations.

**Table-6: Angle of repose- flowability of ofloxacin pellets**

| Formulation | Angle of repose (°)* | Flowability |
|---|---|---|
| B1 | 29.15 ± 0.017 | Good |
| B2 | 24.33 ± 0.025 | Good |
| B3 | 19.34 ± 0.011 | Excellent |
| B4 | 23.12 ± 0.008 | Good |
| B5 | 21.80 ± 0.016 | Good |
| B6 | 17.75 ± 0.027 | Excellent |
| B0 | 35.70 ± 0.037 | Passable |
| * Values indicates (Mean ± S.D.) where samples were analyzed in triplicate. | | |

**BD&TD:**
Table 4.4 represents the bulk density & tapped density of ofloxacin pellet formulations. The bulk and tapped density values of uncoated pellets were 0.651 and 0.855 g/ml. BD & TD values for all coated pellets were 0.675 to 0.801 g/ml and 0.841 to 0.884 g/ml. These results were helpful in calculating compressibility index and Hauser ratio.

**Compressibility index (CI):**CI for pellets formulations were shown in table 4.4. Compressibility index of uncoated pellets was found to be 23.859 with passable flowability. Compressibility index values for all coated formulations were varying in the range of 9.389 to 20.927.

**Hausner ratio (HR):** Hausner ratio for the pellet formulations were shown in table 4.4. Hausner ratio value of uncoated pellets was 1.312 with passable flow properties. Hausner ratios for coated pellets were lies within the range of 1.103 to 1.245.

**Table-7: Micromeretic properties of ofloxacin pellets**

| Formulation | Parameter* | | | | |
|---|---|---|---|---|---|
| | Bulk density | Tapped density | Carr index | Hausner ratio | Flowability |
| B1 | 0.730 | 0.872 | 16.282 | 1.194 | Fair |
| B2 | 0.768 | 0.861 | 10.801 | 1.121 | Good |
| B3 | 0.763 | 0.848 | 10.023 | 1.111 | Excellent |
| B4 | 0.704 | 0.854 | 17.915 | 1.218 | Fair |
| B5 | 0.675 | 0.841 | 20.927 | 1.245 | Fair |
| B6 | 0.801 | 0.884 | 9.389 | 1.103 | Excellent |
| B0 | 0.651 | 0.855 | 23.859 | 1.312 | Passable |
| * Values indicate mean values when sample were analyzed in triplicate. | | | | | |

**Hardness:**
Table 4.5 shows the result obtained for hardness of all the pellet formulations. Hardness of uncoated pellets was found to be about 1.05 kg/cm$^2$. Hardness of all coated pellet formulations varies in the range of 2.65 to 3.15 kg/cm$^2$. The values obtained were in acceptable range.

**Friability:**
Friability of uncoated pellet formulation was found to be around 0.560%. Friability for coated pellets formulations were found in the range of 0.115 to 0.228%. Table 4.5 shows values obtained were within acceptable range.

**Drug content:** Uncoated and coated ofloxacin pellets assay were found in the range of 98.76 to 100.31%. The values obtained were within

acceptable range and with no significant difference found in drug content within formulations (table 4.5).

**Table-8: Physicochemical evaluation of ofloxacin pellets**

| Formulation | Mean pellet size (µ) | Hardness* ($kg/cm^2$) | Friability* (%) | Drug content* (%) |
|---|---|---|---|---|
| B1 | 881 | 2.95 ± 0.15 | 0.127 ± 0.003 | 99.17 ± 1.35 |
| B2 | 884 | 3.00 ± 0.10 | 0.120 ± 0.002 | 98.76 ± 2.33 |
| B3 | 888 | 3.05 ± 0.15 | 0.112 ± 0.003 | 98.91 ± 1.98 |
| B4 | 874 | 2.65 ± 0.20 | 0.215 ± 0.002 | 99.36 ± 3.12 |
| B5 | 878 | 2.85 ± 0.05 | 0.228 ± 0.003 | 99.78 ± 0.85 |
| B6 | 890 | 3.15 ± 0.20 | 0.115± 0.002 | 100.31 ± 3.62 |
| B0 | 864 | 1.05 ± 0.30 | 0.560 ± 0.011 | 100.05 ± 2.87 |
| * Values indicate (Mean ± S.D.) where sample were analyzed in triplicate. | | | | |

## IN VITRO RELEASE STUDIES:

***In vitro* drug release from uncoated pellets in different media**

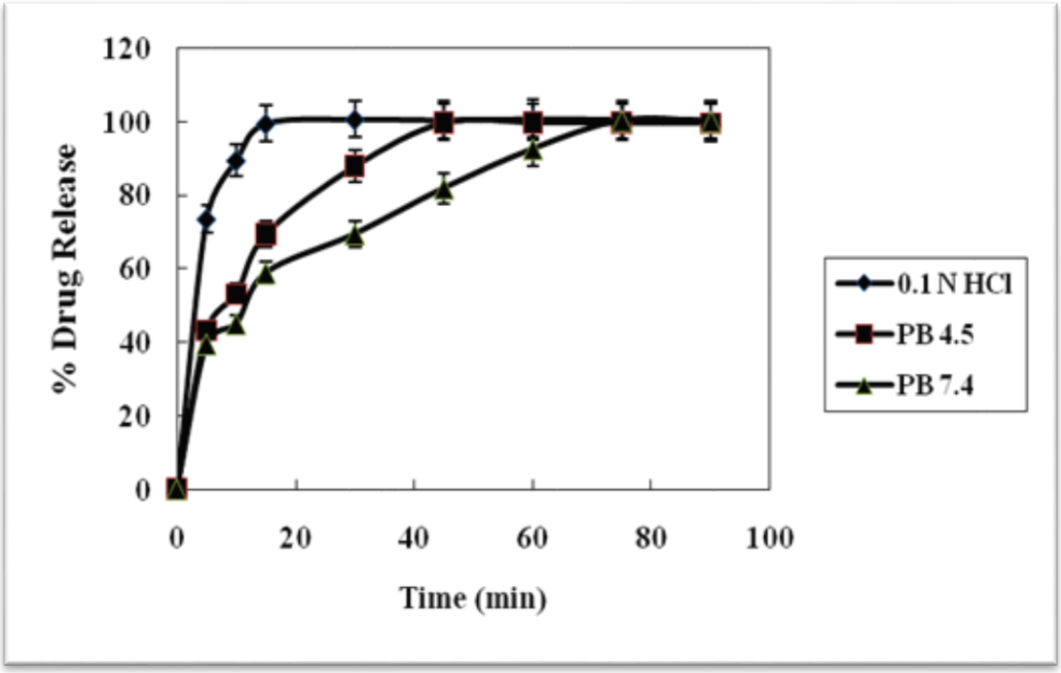
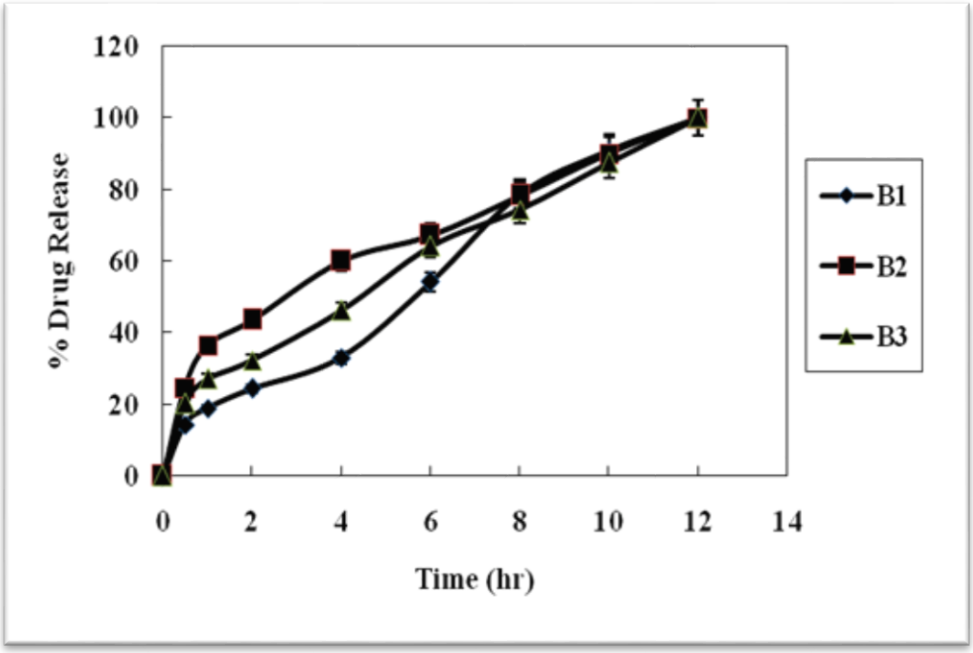



**Figure-9: Release of ofloxacin from uncoated pellets in different media.**

Figure 9 show the ofloxacin release from uncoated pellets was not less than 90% in one hour in 0.1N HCl & pH 4.5 and 7.4. Particularly, uncoated ofloxacin pellets was dissolved in 0.1N hydrochloride acid within 20 min. Hence, it was need to coat the ofloxacin pellets to control its release.




**Dissolution from HMC ofloxacin pellets in various media:**

**Figure-10: Ofloxacin coated pellets dissolution profile in 0.1N HCl with 3 various ratios of SA and PA with 7.5% coating**

Figure 10 shows the coating melt dominated with palmitic acid effectively extended the release of ofloxacin in 0.1N HCl but ofloxacin release proved similar dissolution profiles because of insolubility of stearic & palmitic acid below alkaline pH. Therefore, it was difficult to select the accurate ratio and hence the pellets were analysed in other media.

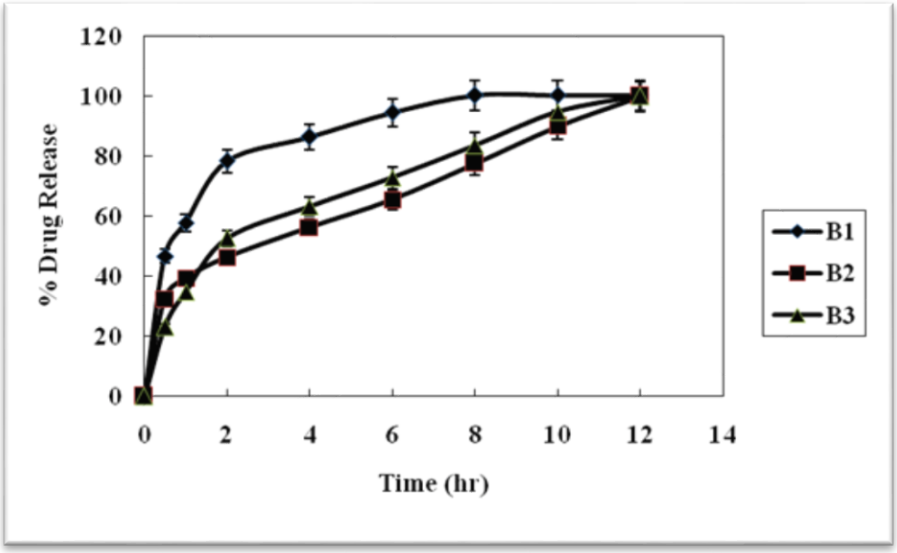



**Figure-11: Release profiles of ofloxacin coated with three different ratios of SA & PA with the coating level of 7.5% in pH 4.5 PB.**

Figure 11 shows the sequence of the release rate in a pH of 4.5 (from the fastest to the slowest) was the pellets with a ratio of 1:5, 1:7.5 and 1:10. It was found that more concentration of stearic acid in formulation means quicker the drug release from pellets formulation.

**Effect of coating concentration on ofloxacin release:**

Figure 4.12 proves ofloxacin dissolved in 1 hour in the dissolution medium with three percent coating concentration (Formulation B4). Five percent coating concentration (Formulation B5) had controlled the ofloxacin release& complete ofloxacin was released in four hours. Ten percent coating concentration (Formulation B6), about twenty two percent drug was dissolved from the formulation in twelve hours& not more than sixty was dissolved at the end of dissolution in twenty four hours. From total coating concentration formulations, formulation B2 proved the better drug dissolution in 0.1N hydrochloric acid, hence 7.5% coating concentration was chosen.

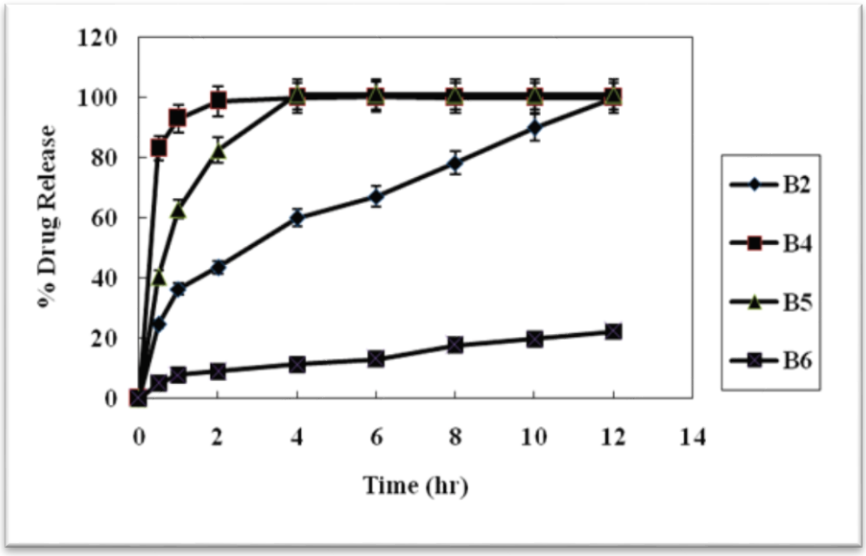



**Figure-12: Effect of coating concentration on ofloxacin release**

**Comparison of Dissolution profiles:**

Bioadhesive and swellable gastro retentive drug delivery system tablet of ofloxacin was designed (Chavanpatil MD. et. al., 2005, Chavanpatil MD. et. al., 2006). Ofloxacin release was regulate dusing polymers having bioadhesive influence which extend the gastric retention time and these benefits assured constant & successful ofloxacin absorption. Ofloxacin release from the tablets in 0.1N HCl at 1, 2, 3, 4, 8, 10 and 12 hr was approximately 27, 38, 50, 65, 75, 88 and 98% respectively (Chavanpatil MD. et. al., 2005, Chavanpatil MD. et. al., 2006).

MR pellets proved similar dissolution profile when compared with above gastro retentive SR tablets for the first eight hours and then more drug was released from the pellets formulations for each time point than gastroretentive tablet formulation. pH changing method was employed by Chavan Patil to investigate his gastric retentive formulation which was primarily kept for two hours in 0.1N HCl dissolution medium. After that tablet was shifted to pH 4.5 dissolution medium for two hours and at the end, tablet was kept in pH 7.4 dissolution medium for twelve hours (Chavanpatil MD. et. al., 2005).

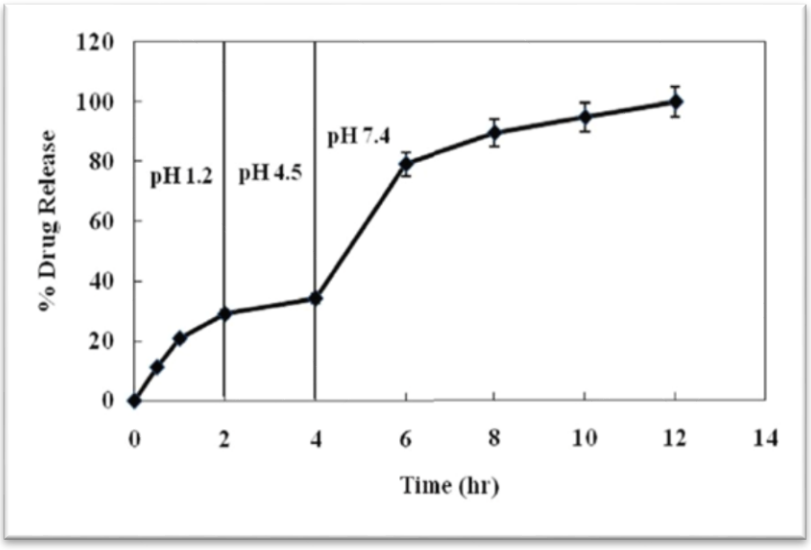



**Figure-13: Release profile of B2 formulation by pH changing method.**

Figure 13 proves the dissolution profile of MR ofloxacin pellets under the condition shown above. In 0.1N HCl dissolution medium for two hours & then in pH 4.5 for another two hours, not more than thirty five percent ofloxacin was dissolved from the pellets formulation which reflected better SR quality. But in pH 7.4 dissolution medium pellets required not more than six hours for the rest drug to be dissolved from the pellets formulation.

**Effect of osmotic pressure on the release of ofloxacin from the pellets:**

Ofloxacin pellets dissolution profiles in 0.1N HCl with0%, 0.9%, 2.0% & 5.0% NaCl are represented in figure 4.14. It was observed that ofloxacin released completely in 2 hrs in 0.1N HCl with different concentration of NaCl.

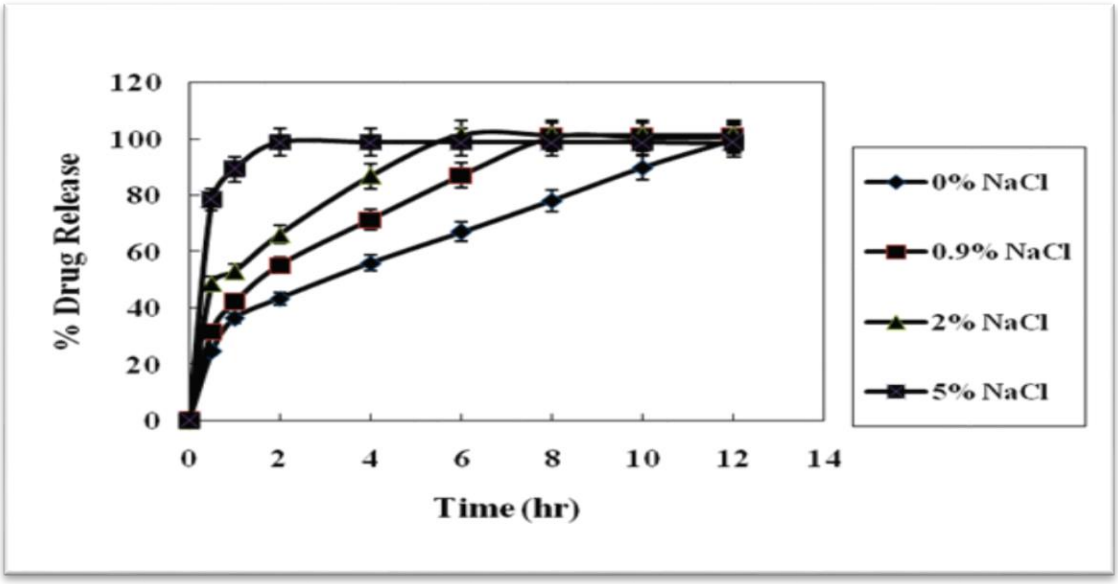



**Figure-14: Release profiles of formulation B2 in 0.1N HCl with different % NaCl**

Above seventy percent ofloxacin dissolved from the formulation in dissolution medium with two percent & five percent NaCl that means about double than the dissolution media without NaCl. More than fifty five percent drug was dissolved in 1 hr in 0.9% sodium chloride dissolution medium. It was observed that more salt concentration in dissolution medium means more drug release. It concludes that drug release enhances with more concentration of osmotic pressure. However, based on literature it was reported that sodium ion do not help to enhance ofloxacin release (Fresta M. et al., 2002). Knop reported that chloride ion with coating material help to enhance the drug dissolution (Knop K., 1996). Hence it was found that releaseof ofloxacin from MR pellets were not because of osmotic pressure.

**Comparison release profile of MR formulations with marketed product:**

Comparison was done more effectively using *f*1 and *f*2 factors. Optimized formulation B2 had *f*1 and *f*2 values, 9.14 and 61.32 respectively (table 3.26).

**Effect of storage temperature on *in vitro* drug release from HMC pellets:**

Formulation B2 was stored at 2-8°C, 25°C and 37°C for 45 days. Dissolution profile in 0.1N HCl indicates that the drug release from B2 formulation stored at 2-8°C is slightly higher than 25°C and 37°C. However, major difference was not found in dissolution profile of drug release which was confirmed by determining similarity and difference factors (table 2.21and table 2.26), and figure 2.17.

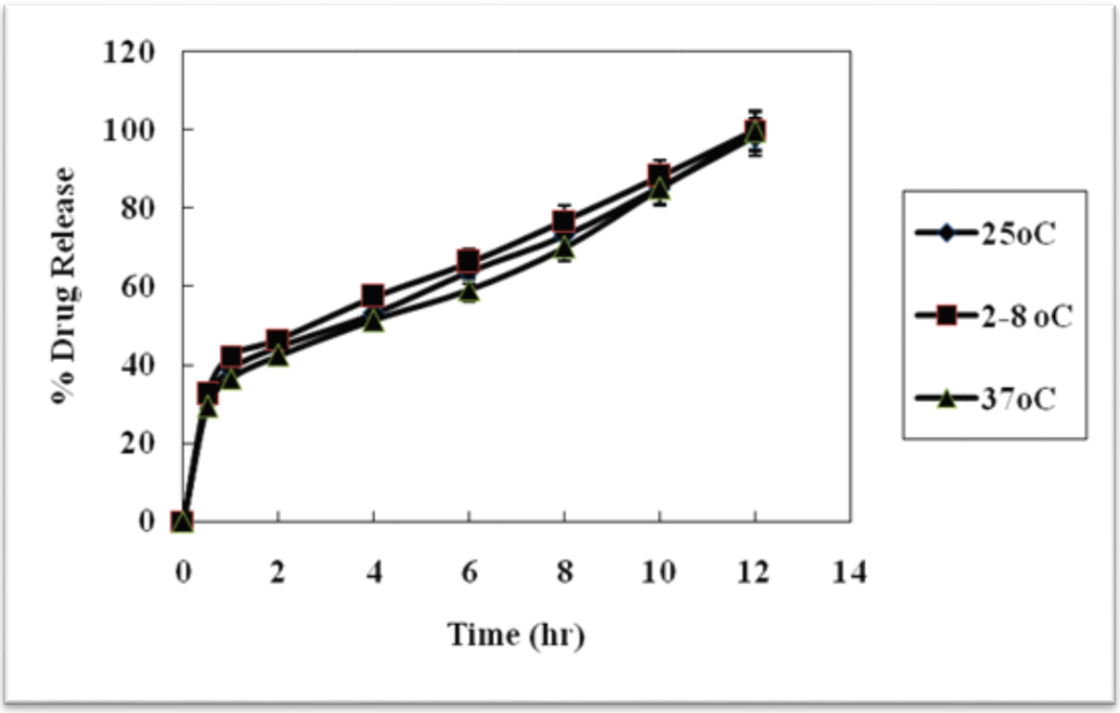



**Figure-15: Effect of storage temperature on drug release from coated pellets.**

**Preparation of two more batches to confirm reproducibility:**

Reproducibility was confirmed by preparing two more batches and comparing their release profile with optimized formulation. Major variation was not found in the ofloxacin dissolution as shown in figure 15.

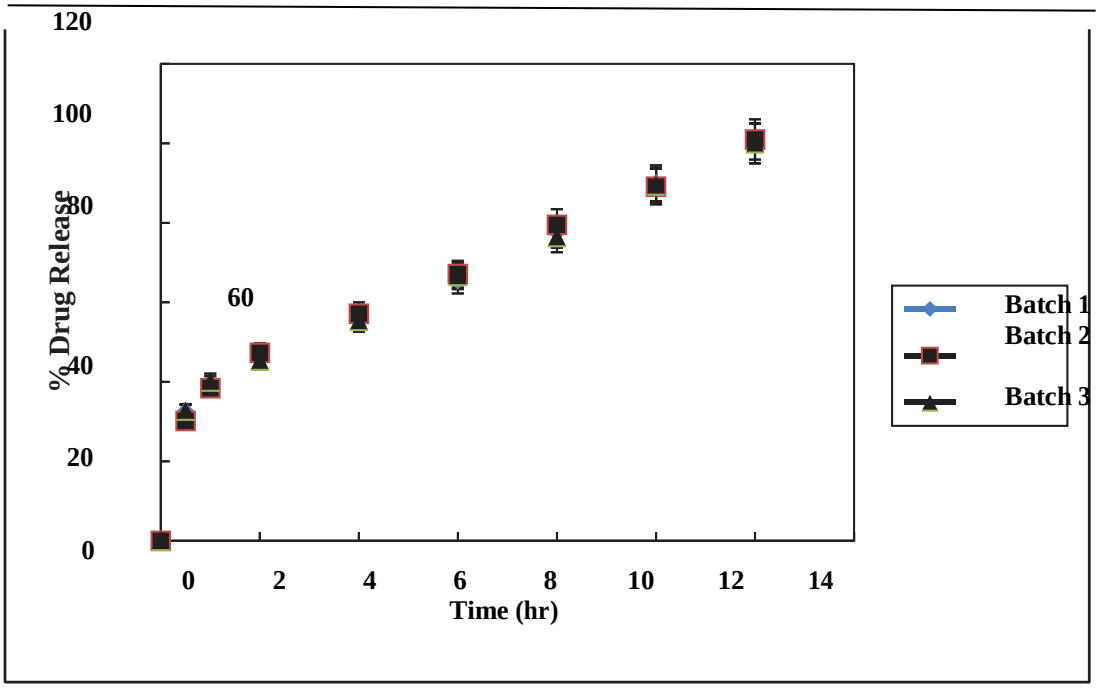



**Figure-16: Release of ofloxacin from reproducibility batches.**

**Kinetic data analysis:**

The release data obtained for six formulations was analyzed using zero &first order model, Higuchi, Hixon-Crowell & Korsmeyer- Peppas model.

**Table-4.6: Kinetic data analysis**

| Formulation | Zero order | | First order | | Higuchi | Korsmeyer-Peppas | | Hixon-Crowell |
|---|---|---|---|---|---|---|---|---|
| | $R^2$ | k0 | $R^2$ | k1 | $R^2$ | $R^2$ | 'n' | $R^2$ |
| B1 | 0.991* | 8.810 | 0.793 | 0.258 | 0.969 | 0.526 | 1.048 | 0.930 |
| B2 | 0.954 | 7.014 | 0.663 | 0.214 | 0.996* | 0.477 | 0.827 | 0.822 |
| B3 | 0.938 | 7.464 | 0.723 | 0.233 | 0.992* | 0.498 | 0.915 | 0.980 |
| B4 | 0.508 | 3.778 | 0.435 | 0.151 | 0.693* | 0.339 | 0.457 | 0.463 |
| B5 | 0.748 | 6.113 | 0.540 | 0.185 | 0.893* | 0.441 | 0.664 | 0.643 |
| B6 | 0.966 | 1.587 | 0.790 | 0.171 | 0.989* | 0.357 | 0.976 | 0.842 |

*Indicates the best fitted kinetic model

Based on the regression coefficient ($R^2$) values, fitting of the release rate kinetic data to the various models reveals for B1 formulation follows zero order release kinetics, whereas all remaining coated formulations were follows Higuchi model (table 4.6). This indicates drug release mechanism from coated pellets was diffusion. Korsmeyer-Peppas equation shows 'n' values lies in the range of 0.5 to 1 indicate drug release mechanism more precisely by non-Fickian diffusion.

**Stability studies:**
Optimized B2 formulation was selected for stability study and it was performed for 2, 4 and 6 months as per ICH guidelines. Formulations were analyzed for physical appearance, assay and dissolution and all results were found within the limit. Hence, product B2 was observed stable for six months.

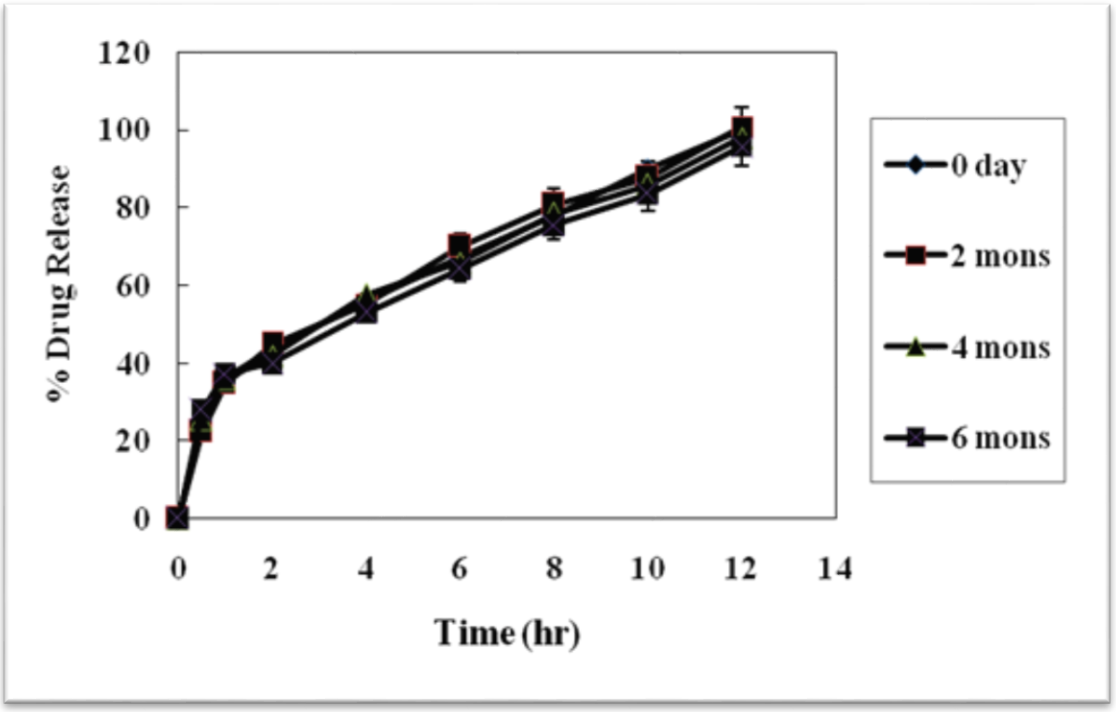



**Figure-17: Stability study of formulation B2 as per ICH guidelines**

## CONCLUSIONS:

In the present investigation a sustained release drug delivery system of ofloxacin using hot melt coating technique was designed successfully. The ofloxacin pellets were prepared by direct pelletization using rotatory shake pelletizer. The pellets prepared were spherical in shape and had smooth surface. Pellets with narrow size distribution, significant physicochemical properties and with fair to excellent flow properties were obtained. Ofloxacin pellets were coated in conventional coating pan with slight modifications and proved to be successful. Further *in vivo* study was needed before commercialization of this product.

The present study has demonstrated that palmitic acid and stearic acid proved their modified release ability. A slower release rate of a drug was observed with increase in coating level. It is worthy of mentioning that proposed technique useful in controlling the release of poorly water-soluble drugs. The result of present study proved that palmitic acid and stearic acid as hot melt coating agent can constitute an excellent alternative to recently used conventional polymers. The hot melt coating technique can be eco-friendly, economic, efficient, simple and rapid tool for the design of modified release dosage form. It is excellent alternative compared to conventional coating technique where solvent evaporation, recovery, treatment and disposal could become very costly and time consuming.

The objective of the present study was to design the SR hot melt coated aceclofenac pellets using CG in combination with ethyl cellulose as HMC agent. Since alone CG cannot provide physical strength and uniform thickness to the coating film Ethyle and cellulose along with CG provide the strength as well as stability. The aceclofenac pellets were successfully prepared by HMC technique. The aceclofenac pellets prepared by this method were spherical in shape and had relatively smooth surface. The aceclofenac pellets were coated with CG using hot-melt coating technique was successful. Hot-melt coating technique presents a faster and cheaper alternative compared to conventional coating methods where solvent evaporation and recovery could become very expensive and time consuming. Dissolution study on the coated aceclofenac pellets showed that the release rate could be controlled using appropriate CG as a coating materials.

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