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# FORMULATION AND EVALUATION OF ENTERIC COATED ELEMENTARY OSMOTIC PUMP (ECEOP) TABLETS OF DICLOFENAC SODIUM

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**Keywords:**

Osmotic device, Elementary osmotic pump, OFAT: One factor at a time, FT-IR: Fourier transform infrared spectroscopy

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**ABSTRACT:** The objective of this study was to formulate a Novel drug delivery device that is capable of releasing the drug in controlled kinetics through the oral route, bypassing the acidic environment of the stomach. Therefore, it was planned to develop an osmotic device with an enteric coating. It was projected to enhance the strength of the semi-permeable membrane for the osmotic device to control drug release for a longer time at controlled release kinetics. The formulations were designed and optimized by using OFAT design to find out the best formulation. The drug release rate was taken up to 8 h, and a comparative study of drug release with a marketed product was carried out. The drug release kinetics showed the optimized device to follow zero-order release kinetics. The FT-IR studies revealed that no physicochemical interaction between excipients and drugs. Stability studies showed that optimized formulation was stable. The observed drug release pattern was found significantly similar at a later stage to release the pattern of a marketed product. The formulated tablets of Diclofenac Sodium were found to be therapeutically safe, which did not release any drug content in an acidic medium for a predetermined time, but it released the drug in a sustained manner in alkaline medium. It was capable of releasing the drug 80.33% in 6 h, which is almost similar to a film-coated sustained-release marketed formulation, which was capable of releasing the drug 82.78% in 6 h.

**INTRODUCTION:** Osmotic pumps are controlled drug delivery devices based on the principle of osmosis. It can provide continuous delivery of a chosen therapeutic agent at a predetermined rate and predictable kinetics throughout the GI transit. An elementary osmotic pump was developed by Alza named OROS®, for controlled release oral drug delivery formulations [1].

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The oral osmotic pump tablets have many advantages, such as easy formulation and simple operation, zero-order delivery rate, improved patient compliance with reduced dosing frequency [2]. Moreover, they are not expensive, and their industrial adaptability vis-a-vis production scale-up is easy.

The release rate from these controlled drug delivery devices is dependent on the coating thickness, level of leachable components in the coating, solubility of the drug in the tablet core, and difference in osmotic pressure across the semipermeable membrane but is independent of the pH and agitation of the release media [3]. Diclofenac sodium is a phenylacetic acid derivative, 2-(2- (2, 6-

dichlorophenylamino) phenyl) acetic acid, sodium, and it is a prototypical non-steroidal anti-inflammatory (NSAID) analgesic drug with cyclo-oxygenase inhibition activity. This drug is generally used to treat pain, rheumatoid arthritis, osteoarthritis, dysmenorrhea, ocular inflammation, ankylosing spondylitis and actinic keratosis [4].

Diclofenac sodium has a short biological half-life, which is about 2 h and it absorbs throughout the intestinal tract. The drug shows linear pharmacokinetics, which is suitable for oral controlled-release tablets. It would be advantageous to slow down its release in the GI tract not only to prolong its therapeutic action but also to minimize possible side effects of Diclofenac sodium [5]. But long-term use of Diclofenac sodium causes an increased risk of upper gastrointestinal bleeding, ulceration, and perforation of the stomach, which can be fatal. Being the osmotic device was designed to enteric-coated the most common adverse effects and contradictions of Diclofenac sodium could be prevented as the device didn't release the drug in the stomach environment. The drug release from the formulated ECEOP tablets was compared with a marketed formulation in order to analyze the release pattern.

## MATERIALS AND METHODS:

**Materials:** Diclofenac sodium was purchased from Universal Chemicals (Kolkata, India). Sodium chloride and Ethyl cellulose were purchased from S.D Fine Chemicals (Mumbai, India). Lactose monohydrate was purchased from HiMedia Laboratories Pvt. Ltd. (Mumbai, India). Sodium Dodecyl sulfate was purchased from Merck Specialities Private Limited (Mumbai, India). Sodium carboxymethyl cellulose, Magnesium stearate and talc were purchased from Loba Chemie Pvt. Ltd. (Mumbai, India). Polyvinyl Pyrrolidone K30 was purchased from Sisco Research Laboratories Pvt. Ltd. (Mumbai, India). Cellulose acetate was purchased from Eastman (New Delhi, India).

Cellulose acetate ahthalate was purchased from spectrochem Pvt. Ltd. (Mumbai, India). Ethanol was purchased from Changshu Hongsheng Fine Chemicals (Changshu City). Methanol was purchased from Qualigens Fine Chemicals (Mumbai, India). Voveran 100 SR tablets were obtained from a retail pharmacy. All other reagents and solvents used were of analytical grade.

**Fourier Transform Infrared Spectroscopy (FT-IR):** The process consisted of dispersing the sample (crude drug, physical mixture of drug and excipients) in potassium bromide and it was compressed into discs by creating a pressure of 5 tons in a hydraulic press for 5 min. The pellet was kept in the path of light and the spectrum was recorded [6].

**Formulation of Enteric Coated Elementary Osmotic Pump Tablet:**

**Preparation of Core Tablets:** The core tablets were prepared by wet granulation method. Drug and all the excipients except talc were accurately weighed. The ingredients were uniformly mixed in a mortar with a pestle for 15 min. To the resultant mixture, warm water was added to form a coherent mass. The coherent mass was passed through 16 mesh screen to form granules. The wet granules were dried at 60 ℃ in a hot air oven for about 2 h. The dried granules were passed through sieve no. 20 to break the lumps and to get uniform particle size of granules. Talc was passed through sieve no. 40 and mixed with dried granules. The lubricated granules were compressed into round-shaped tablets by using single punch standard compression machine [7].

**TABLE 1: COMPOSITION OF CORE DICLOFENAC SODIUM TABLETS**

| S. no. | Ingredients | Amount (mg) |
|---|---|---|
| 1 | Diclofenac sodium | 100 |
| 2 | Sodium chloride | 133.5 |
| 3 | Lactose monohydrate | 100 |
| 4 | Sodium dodecyl sulfate | 66.5 |
| 5 | Sodium carboxymethyl cellulose | 100 |
| 6 | Polyvinyl pyrrolidone K30 | 33.35 |
| 7 | Magnesium stearate | 6.65 |
| 8 | Talc | 60 |
| 9 | Warm water | q.s. |
| | Total weight | 600 mg |

**Formulation and Development:**

**Designing of Composition for the Coating Solution:** Ethylcellulose and cellulose acetate were used to formulate a coating solution. These two materials were used together in three different ratios to measure the maximum rupturing time of the semi-permeable membrane. Ethanol was used as solvent, and glycerol was used as a plasticizer.

**TABLE 2: DIFFERENT RATIOS USED FOR COATING MATERIALS**

| S. no. | Coating materials | C1 | C2 | C3 |
|---|---|---|---|---|
| 1 | Ethyl cellulose : Cellulose acetate | 1 : 1 | 1 : 3 | 3 : 1 |

**Optimization of Amount of Plasticizer:** Glycerol has good plasticizer properties. To enhance the elasticity of the osmotic system. Glycerol was added at different amounts in the selected coating solution.

**TABLE 3: DIFFERENT AMOUNTS USED FOR PLASTICIZER**

| S. no. | Plasticizer | P1 | P2 | P3 | P4 | P5 |
|---|---|---|---|---|---|---|
| 1 | Glycerol | 0.35 ml | 0.5 ml | 0.6 ml | 0.75 ml | 0.9 ml |

**Coating of Core Tablets:** Compressed tablets were coated with an appropriate coating solution by using a dipping method. After getting coated the tablets were dried at 40-50 ℃ for about 1-2 h to remove residual solvent [7].

**TABLE 4: COMPOSITION OF COATING SOLUTION**

| S. no. | Ingredients | Amount |
|---|---|---|
| 1 | Cellulose acetate | 3.45 g |
| 2 | Ethyl cellulose | 1.15 g |
| 3 | Glycerol | 0.75 ml |
| 4 | Ethanol | 100 ml |

**Designing an Orifice:** An orifice was designed on the surface of each coated tablets using a needle of an insulin syringe.

**Enteric Coating of the Tablets:** The tablets were made enteric-coated by using appropriate coating solution of Cellulose acetate phthalate. After coating, the tablets were dried at 50-60 ℃ for about 1-1.5 h to remove residual solvent.

**TABLE 5: COMPOSITION OF ENTERIC COATING SOLUTION**

| S. no. | Ingredients | Amount |
|---|---|---|
| 1 | Cellulose acetate phthalate | 10 g |
| 2 | Ethanol : Acetone (1:3) | 100 ml |

**Powder Flow Properties:**

**Bulk Density:** Bulk Density ($g/cm^3$) is a term obtained by dividing the weight of powder by bulk volume of powder. 25 g of the drug, powder blend and granules were taken individually into a measuring cylinder of 100 ml.

The cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2-second intervals for three times. Bulk Density is calculated using the following formula [8]

$$\text{Bulk Density } (\rho b) = W/V_b$$

Where, W is the weight of the powder in g, $V_b$ is the bulk volume of the powder in $cm^3$.

**Tapped Density:** Tapped Density ($g/cm^3$) is a term obtained by dividing the weight of powder by tapped volume of powder. 25 g of the drug, powder blend and granules from was taken individually into a 100 ml measuring cylinder.

The cylinder was allowed to fall under its own weight onto a hard surface from the height of 2.5 cm at 2-sec intervals for 500 times. Tapped Density is calculated using the following formula [8]

$$\text{Tapped Density } (\rho t) = W/V_t$$

Where, W is the weight of the powder in g, $V_t$ is the tapped volume of the powder in $cm^3$.

**Carr's Index:** It is an indirect measure of Bulk Density, size, and shape, surface area, moisture content, and cohesiveness. It is expressed in percentage and can be calculated by following equation [8]

$$\text{Carr's Index (CI)} = (\rho_t - \rho_b) / \rho_t \times 100$$

Where, $\rho_b$ is the bulk density in $g/cm^3$, $\rho_t$ is the tapped density in $g/cm^3$.

**Hausner's Ratio:** It is measured by the ratio of tapped density to bulk density. Ideal range should be between 1.2 and 1.5. It is calculated by the following formula [8]

$$\text{Hausner's Ratio} = \rho_t / \rho_b$$

Where, $\rho_b$ is the bulk density in $g/cm^3$, $\rho_t$ is the tapped density in $g/cm^3$.

**Angle of Repose:** The angle of repose of the drug, powder blend, and granules was individually determined by the fixed funnel method, which employs a funnel that is secured with its tip at 2 cm above graph paper that is placed on a flat horizontal surface. From the radius of the base of the conical pile, angle of repose can be determined using the following equation [8].

$$\text{Angle of Repose } (\theta) = \tan^{-1} (h/r)$$

Where, h is the height of the pile of powder in cm, r is the radius of the pile of powder base in cm.

**Evaluation of Enteric Coated Elementary Osmotic Pump Tablets:**

**Uniformity of Weight:** Ten tablets were selected at random from the prepared batch. The individual tablets were weighed. The average weight was determined. The individual weight of tablets was compared with the average weight [9].

**Diameter and Thickness:** Five tablets from the prepared batch were randomly selected. The diameter and thickness of the tablets were measured [9].

**Hardness:** The resistance of tablets to crushing or breakage during storage, transportation, and handling before usage was measured using the Pfizer hardness tester. Five tablets from the prepared batch were randomly selected and tested. It is expressed in $Kg/cm^2$ [9].

**Friability:** Ten tablets were randomly selected, weighed, and placed in a Roche Friabilator. The apparatus was rotated at 25 rpm for 4 min. After revolutions, the tested tablets were deducted, and again they were weighed. The percentage friability was measured by using the following formula [9]

$$\text{Percentage Friability} = (W_0 - W_F / W_0) \times 100$$

Where, $W_0$ is the initial weight of tablets, $W_F$ is the final weight of tablets.

***In-vitro* Dissolution Studies:** Drug release studies were carried out using USP dissolution test apparatus (Apparatus II paddle type). Two dissolution mediums were used to evaluate the drug release. One medium was 900 ml of phosphate buffer pH 6.8, and another was 900 ml of simulated gastric fluid pH 1.2. The release was performed at 37 ± 0.5 °C, with a rotation speed of 100 rpm. 10 ml samples were withdrawn at predetermined time intervals and replaced with fresh medium. The samples were filtered through Whatman filter paper and analyzed after appropriate dilution by UV spectrophotometer at 285 nm [10].

**Drug Release Kinetics Study:** *In-vitro* release data of the optimized formulation were fitted to various mathematical models such as zero order, first order, Higuchi release kinetics, Korsmeyer – Peppas release kinetics, Hixson – Crowell release kinetics to describe the kinetics of drug release.

**Zero Order Release Kinetics:** The graph was plotted as time in minute *vs.* percentage drug release, the slope gave the rate of kinetics. It is generally represented by [11]

$$C = K_0 t$$

Where, '$K_0$' is the zero-order constant, 'C' is the concentration of the drug, 't' is the time.

**First Order Release Kinetics:** The graph was constructed for a time in min *vs.* percentage log drug remaining. The equation is [11]

$$\log C = \log C_0 - K_1 t/2.303$$

Where, '$C_0$' is the initial concentration of the drug, '$K_1$' is the first-order rate constant, 't' is the time.

**Higuchi Release Kinetics:** The plot was constructed between square root times *vs.* cumulative percentage drug release.

This type of graph is specially employed for several types of modified release pharmaceutical dosage forms. It is expressed as [11]

$$Q = K\sqrt{t}$$

The slope gave the rate constant of drug release in time t.

**Korsmeyer-Peppas Release Kinetics:** The release kinetics equation for drug release is expressed as [12]

$$M_t/M_\alpha = K_t n$$

$$\text{Log } (M_t/M_\alpha) = n\log t + \log K$$

Where, '$M_t/M_\alpha$' is the amount of drug release in time t. The slope gave the value of n. The release kinetics was obtained from the intercept.

**Hixson – Crowell Release Kinetics:** The graph was plotted as time in minute *vs.* cube root of percentage drug release remaining. The equation is expressed as [12]

$$(W_0)^{1/3} - (W_t)^{1/3} = Kst$$

Where, '$W_0$' is the initial amount of drug, '$W_t$' is the remaining amount of drug at time t, '$K_S$' is the constant incorporating surface-volume retention.

Data were treated according to the release kinetics models using the least square method of analysis. The best goodness of fit test ($R^2$) was taken as criteria for selecting the most appropriate model.

**Accelerated Stability Study:** Stability studies were carried out on optimized formulation. The tablets were stored at 40 ± 2 ℃ and 75% ± 5% RH for the duration of one month.

After one-month samples were withdrawn and tested for various parameters like visual appearance, loss on drying *in-vitro* dissolution study [13].

## RESULTS AND DISCUSSION:

**TABLE 6: IDENTIFICATION OF DRUG BY PERFORMING SEVERAL MONOGRAPHIC TESTS**

| Tests | Expected Result | Obtained Result |
|---|---|---|
| To 1 ml of a 0.4% w/v solution of Diclofenac sodium in Methanol add 1 ml of Nitric acid | Dark red color develops | Dark red color was developed |
| Appearance of solution: A 5.0% w/v solution of Diclofenac sodium in Methanol | Clear | Clear |
| pH of 1.0% w/v solution of Diclofenac sodium | 6.5 – 8.5 | 7.4 |
| Loss on Drying: 1.0 g Diclofenac sodium is dried in a hot air oven at 105 ºC for 3 h | Not more than 0.5% | 0.4% |
| Light Absorption: Absorbance of a 5.0% w/v solution of Diclofenac sodium in Methanol at about 440 nm | Not more than 0.050 | 0.043 |
| Assay: Weigh accurately about 0.2 g and dissolve in 50 ml of anhydrous glacial acetic acid. Titrate with 0.1 M perchloric acid, determine the endpoint potentiometrically. Carry out a blank titration | ----- | 97.01 % |

**Identification and Compatibility of Drug and Excipients using FT-IR:** The identification of the drug and the compatibility between the excipients was carried out using FTIR. The FTIR characteristics of Diclofenac sodium resemble almost the same with the spectra of authentic sample of Diclofenac sodium. By analyzing the FTIR Spectra, it is clearly evident that the physical mixtures of Diclofenac with different excipients showed the presence of Diclofenac characteristics bands at their same wavenumber. This indicates the absence of chemical interaction between the drug and the excipients. The FTIR spectrum and results of the drug are given below.

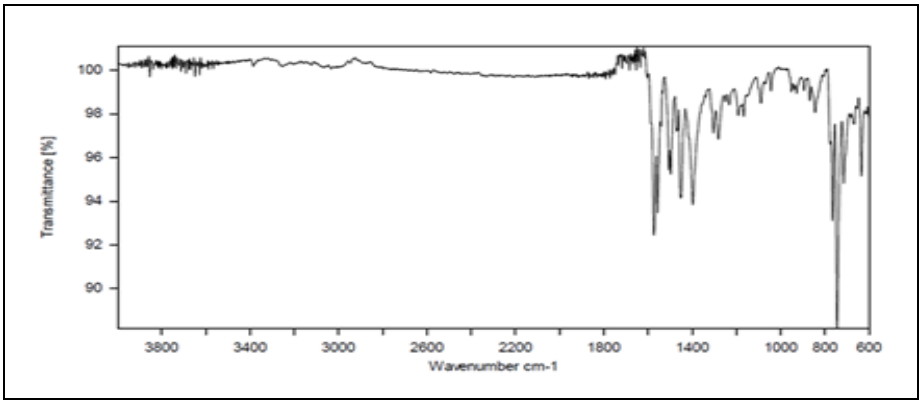



**FIG. 1: FTIR SPECTRUM OF DICLOFENAC SODIUM**

**TABLE 7: FTIR SPECTRUM INTERPRETATION OF DICLOFENAC SODIUM**

| Wave Number ($cm^{-1}$) | Interpretation |
|---|---|
| 3381.00 | NH stretching |
| 1647.00 | C = O |
| 1564.00 | NH bending |
| 1453.00 | CH bending |
| 750.00 | - Cl stretching |

**Powder Flow Properties:** The obtained result of pre-compression parameters for the drug, formulated powder blends, and granules is given below. The drug and the formulated blends showed good flow property. But the flow property of granules was excellent.

**TABLE 8: PRECOMPRESSION STUDIES OF THE DRUG, POWDER BLENDS, GRANULES**

| Sample | Bulk Density ($g/cm^3$) | Tapped Density ($g/cm^3$) | Carr's Index (%) | Hausner's Ratio | Angle of Repose (θ) |
|---|---|---|---|---|---|
| Drug | 0.663 | 0.768 | 13.67 | 1.16 | 31.32 |
| Powder blends | 0.622 | 0.730 | 14.79 | 1.17 | 35.44 |
| Granules | 0.479 | 0.534 | 10.29 | 1.11 | 19.43 |

**Standard Curve of Diclofenac Sodium:** The absorbance of the drug in phosphate buffer pH 6.8 was measured at a wavelength of 285 nm. The standard curve of Diclofenac sodium in Phosphate buffer pH 6.8 was found linear, starting from the origin. The curve obeys Beer-Lambert Law.

**TABLE 9: STANDARD CURVE OF DICLOFENAC SODIUM**

| S. no. | Concentration (mcg/ml) | Absorbance at 285 nm Phosphate buffer pH 6.8 |
|---|---|---|
| 1 | 1 | 0.033 |
| 2 | 2 | 0.072 |
| 3 | 3 | 0.111 |
| 4 | 4 | 0.144 |
| 5 | 5 | 0.161 |

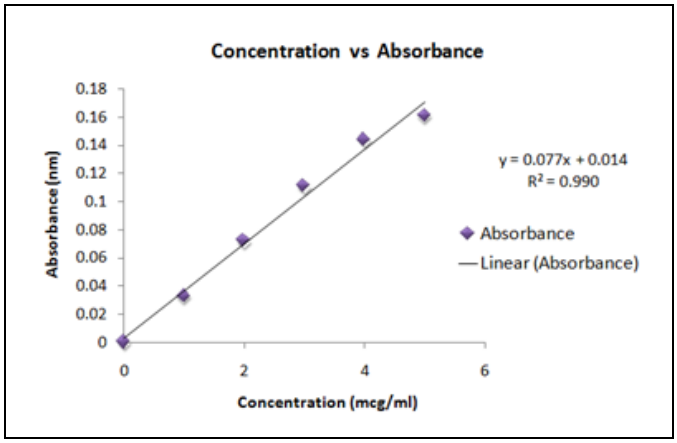



**FIG. 2: STANDARD CURVE OF DICLOFENAC SODIUM IN PHOSPHATE BUFFER pH 6.8**

**Formulation and Development:**

**Designing of Composition for the Coating Solution:**

**Ethyl Cellulose:** Cellulose acetate (1:3) in Ethanol (100 ml) – this coating solution provided the maximum rupturing time 4 h and can withstand the osmotic pressure for a longer time in comparison with other compositions. So, this coating composition was selected for the coating of the final batch of tablets.

**Optimization of Amount of Plasticizer:** Glycerol is used as a plasticizer to provide the elasticity for expansion of semi-permeable membrane. By using 0.75 ml Glycerol in the C3 coating solution, the maximum rupturing time 5 h was found.

**Ethyl Cellulose:** Cellulose acetate (1:3) in Ethanol (100 ml) with Glycerol (0.75 ml) – this coating solution was capable of providing the maximum mechanical strength. So, this coating composition was selected for coating of final batch of tablets.

**TABLE 10: OPTIMIZATION OF RUPTURING TIME OF SEMIPERMEABLE MEMBRANE**

| S. no. | Materials | Rupturing Time |
|---|---|---|
| 1 | Ethyl cellulose : Cellulose acetate (1 : 1) in Ethanol | 3.5 h |
| 2 | Ethyl cellulose : Cellulose acetate (1 : 3) in Ethanol | 4 h |
| 3 | Ethyl cellulose : Cellulose acetate (3 : 1) in Ethanol | 2 h |

**TABLE 11: OPTIMIZATION OF AMOUNT OF PLASTICIZER**

| S. no. | Amount of Glycerol | Rupturing time |
|---|---|---|
| 1 | 0.35 ml | 4 h |
| 2 | 0.50 ml | 4 h |
| 3 | 0.60 ml | 4.5 h |
| 4 | 0.75 ml | 5 h |
| 5 | 0.90 ml | 4 h |

**Uniformity of Weight:** ECEOP tablets of Diclofenac sodium were subjected to weight variation test. The tablets were found to be uniform in weight, and the weight ranged between 0.706 g to 0.709 g.

**Diameter and Thickness:** The diameter of the tablets ranged between 12.0 mm to 12.1 mm. The thickness of the tablets ranged between 3.0 mm to 3.5 mm. The ECEOP tablets were uniform in diameter and thickness.

**Hardness:** The hardness of ECEOP tablets ranged between 5.4 $kg/cm^2$ and 5.6 $kg/cm^2$. Hence, the tablets were hard enough to withstand stress during transport and handling.

**Friability:** The friability of ECEOP tablets was found to be 0.80%. Hence, the tablets had enough strength to withstand any mechanical shocks such as handling in manufacturing, packaging, and shipping.

***In-vitro* Dissolution Studies:** The result of the dissolution study of the ECEOP tablets is given below.

**TABLE 12: *IN-VITRO* DRUG RELEASE OF ECEOP TABLETS**

| Dissolution medium | Time (min) | % Cumulative drug release (%CDR) |
|---|---|---|
| Acid buffer pH 1.2 | 0 | 0 |
| | 30 | 0 |
| | 60 | 0 |
| | 90 | 0 |
| | 120 | 0 |
| | 150 | 0.12 |
| | 180 | 2.99 |
| | 210 | 8.14 |
| | 240 | 15.15 |
| Phosphate buffer pH 6.8 | 270 | 22.40 |
| | 300 | 30.47 |
| | 330 | 38.76 |
| | 360 | 47.53 |
| | 390 | 56.88 |
| | 420 | 65.17 |
| | 450 | 72.69 |
| | 480 | 80.33 |

**Drug Release Kinetics Study:** When the data was plotted according to the various release kinetics equations, the ECEOP tablets showed poor linearity for all release kinetics as compared to zero order release kinetics; whereas the regression value for zero-order equation indicated that the drug release from optimized formulation was independent of drug concentration. The drug release was totally dependent on the release mechanism of the delivery device based on osmotic pressure mechanism developed due the osmogen.

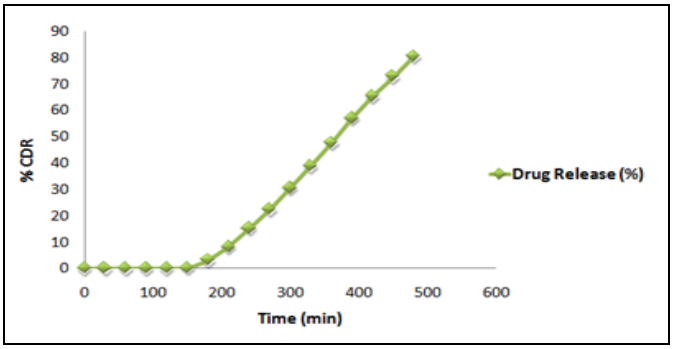
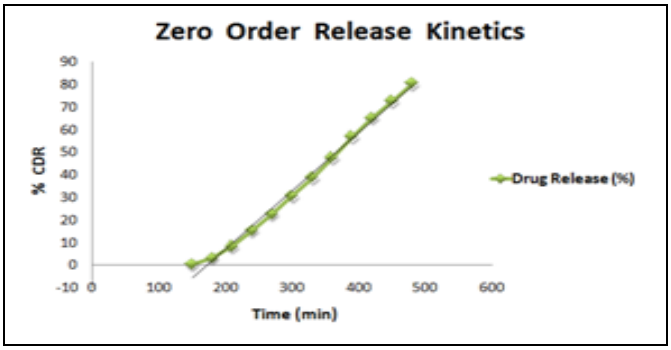
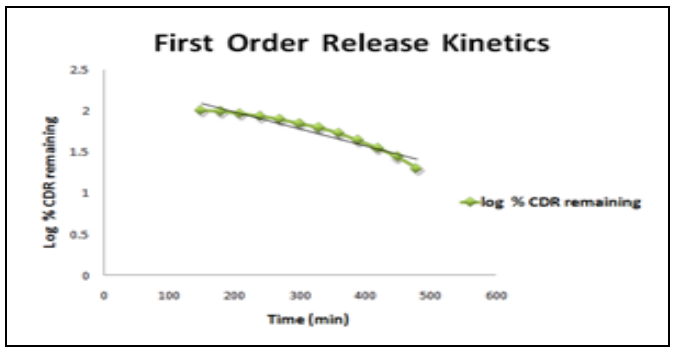
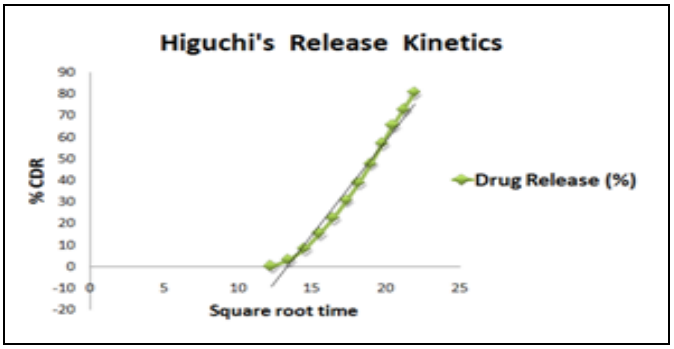
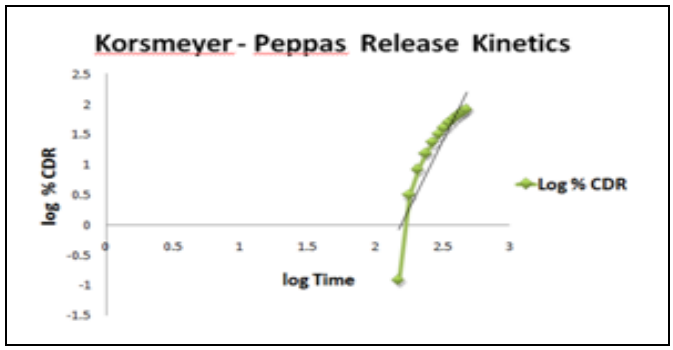



**FIG. 3: *IN-VITRO* DRUG RELEASE STUDY OF ECEOP TABLETS**



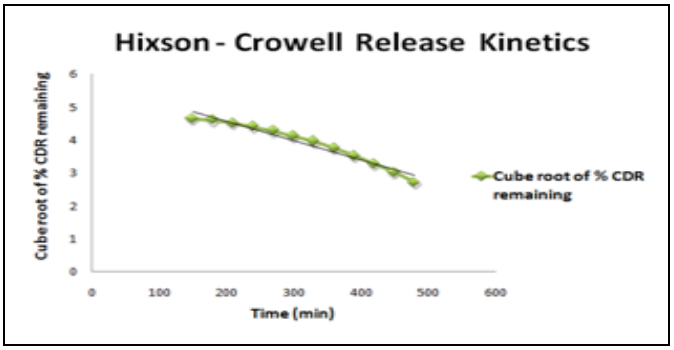




**FIG. 4: DIFFERENT RELEASE KINETICS OF ECEOP TABLETS**

**TABLE 13: REGRESSION VALUE OF DIFFERENT RELEASE KINETICS**

| S. no. | Release Kinetics | Regression Value ($R^2$) |
|---|---|---|
| 1 | Zero-order | 0.992 |
| 2 | First-order | 0.929 |
| 3 | Higuchi | 0.974 |
| 4 | Korsmeyer - Peppas | 0.824 |
| 5 | Hixson – Crowell | 0.960 |

**Comparative Analysis of Drug Release:** In order to check the similarity of the drug release with a controlled release product (Voveran 100 SR). Since the marketed formulation was a film-coated product, the drug release in acidic pH was not carried out, and the dissolution study was initiated at alkaline pH with ECEOP tablets.

The drug release from ECEOP was higher but at a constant linear rate in comparison to the marketed tablet, which initially was slow but superimposed at a later stage. It is clear that the zero-order drug release of ECEOP was responsible for such a release process.

**TABLE 14: COMPARISON BETWEEN DRUG RELEASE STUDY OF FORMULATED ECEOP TABLET AND MARKETED PRODUCT**

| Dissolution Medium | Time (min) | % Drug Release | |
|---|---|---|---|
| | | ECEOP Tablet | Marketed Product |
| Phosphate Buffer pH 6.8 | 30 | 0.12 | 0.819 |
| | 60 | 2.99 | 2.34 |
| | 90 | 8.14 | 4.33 |
| | 120 | 15.15 | 7.28 |
| | 150 | 22.40 | 12.06 |
| | 180 | 30.47 | 17.79 |
| | 210 | 38.76 | 25.27 |
| | 240 | 47.53 | 34.74 |
| | 270 | 56.88 | 45.61 |
| | 300 | 65.17 | 57.53 |
| | 330 | 72.69 | 70.03 |
| | 360 | 80.33 | 82.78 |

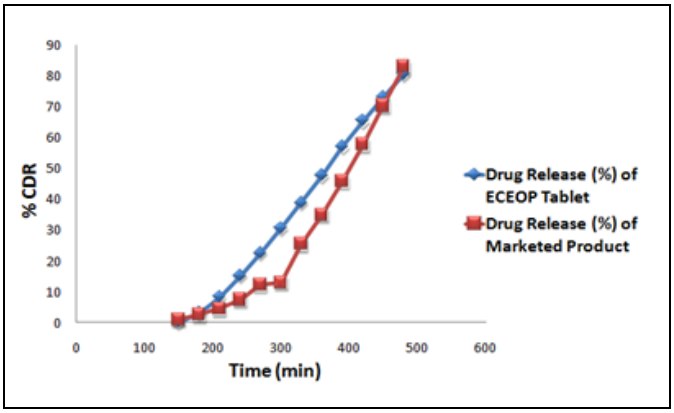



**FIG. 5: COMPARISON BETWEEN DRUG RELEASE STUDY OF FORMULATED ECEOP TABLET AND MARKETED PRODUCT**

**Accelerated Stability Study:** The study showed that there was no observable degradation within the stipulated time. The study confirmed that the optimized formulation was stable.

**TABLE 15: EVALUATION TESTS RESULTS OF OPTIMIZED ECEOP TABLETS AFTER STABILITY STUDY**

| S. no. | Tests | Results |
|---|---|---|
| 1 | Visual appearance | No change |
| 2 | Hardness | 5.4 kg/cm$^2$ |
| 3 | Friability | 0.82 % |
| 4 | % Drug release after 6 h | 79.98 % |
| 5 | % Assay | 96.58 % |

**CONCLUSION:** The observed drug release rate from formulated ECEOP tablets was 80.33% in 8 h **Table 12**. The drug release was not dependent on the concentration of the drug, which was totally dependent on the release mechanism of the delivery device. The semipermeable membrane developed was capable of withstanding sufficient osmotic pressure and of producing maximum elasticity. The release pattern of the drug in a sustained manner from the optimized device was similar to the marketed formulation **Table 14**. Accelerated stability study of the formulated ECEOP tablets of Diclofenac sodium ensured there was not any crucial changes in any results **Table 15** and also unchanged in physical appearance.

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