WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 12, Issue 14, 879-898. Research Article ISSN 2277–7105

DESIGN AND *IN-VITRO* EVALUATION OF OSMOTICALLY CONTROLLED RELEASE TABLET OF INDOMETHACIN

***Satyansh Kumar Singh, Vivek Kumar Patel and Rajeev Shukla**

Sheat College of Pharmacy, Gahni, Varanasi U.P., India.

Article Received on
28 June 2023,

Revised on 18 July 2023,
Accepted on 08 August 2023

DOI: 10.20959/wjpr202314-29012

***Corresponding Author**
Satyansh Kumar Singh
Sheat College of Pharmacy,
Gahni, Varanasi U.P., India.

ABSTRACT

Objectives: The aim of the present study was to prepare controlled porosity osmotic pump (CPOP) of indomethacin in order to reduce the dosing frequency and hence decrease side effect. So that it can improve the therapeutic efficiency of indomethacin by maintaining constant plasma level over 12 hrs. **Materials and Methods:** Formulation were designed by preparation of controlled porosity osmotic tablet firstly, by direct compression then coating material was prepared and core tablets were coated using coating pan to get osmotically controlled release tablet. The controlled porosity osmotic drug delivery system consists of the core tablet containing drug and osmogenes along with other excipients and finally coated with polymer mixed with pore forming agent which is water soluble in nature. **Results:** The optimized formulation F-7 of osmotically controlled release tablet had shown 96.8% drug release in 12 hrs. Initially at 3 hrs drug relase was found to be 26.3% due to osmotic agent used. **Conclusion:** (F1-F10) indicates that the controlled porosity osmotic pump is suitable for delivery of indomethacin for more than 12 hours. The controlled porosity osmotic pump is cost effective technology along with reduced dosing frequency and increased patient compliance. The comparision of release profile of EOP with CPOP (F1-F10) indicates that the CPOP is suitable for delivery of indomethacin for more than 12 hours. It can be concluded that CPOP is ideal for the delivery of the drug where release of the drug is required to be for more than 12 hours.

KEYWORDS: Controlled, osmotic, Porosity, Indomethacin, Coating.

INTRODUCTION

A major drawback of conventional drug delivery system is no control over the drug to the target site in effective concentration.[1] Many times dozing to patient causes inconvenience of

drug delivery and causing an uneven plasma drug concentration which leads to side effect as well as less toxicity.[2] However, fluctuation of plasma drug concentration caused by conventional tablet can cause serious side effect.[3] Hence, to reduce the limitations of conventional drug delivery system, researcher's attention goes towards novel drug delivery system.[4] Developing a novel drug delivery system that is sustained release and controlled release formulation can improve efficacy, safety, product shelf life and patient compliance these advantages attract so much attention of researches.[5] Because these formulations maintain steady state of plasma drug concentration and reduce the dose strength as well as frequency of dose.[6] Among these systems, osmotic controlled release system is much more superior than other because of its more stable plasma drug concentration and better in-vitro in-vivo correlation, provide measured amount of drug over a prolonged period of time.[7] In osmotically control release system, controlled porosity osmotic pump (CPOP) is better than elementary osmotic pump (EOP) and other like systems. CPOP system free from influence of physiological factors like pH and GIT peristalsis and provide zero order release.[8] However conventional EOP not suitable for release of drug in controlled manner hence this work done on CPOP formulation in comparison with EOP. To get therapeutic effect of active ingredient in constant manner there is need of zero order release of drug from the system hence CPOP provide zero order release that is controlled release.[9] CPOP gives independent delivery of physiological factor of GIT and drug concentration.[10] Drug release in CPOP depends on level of leachable constituent in coating, thickness of coating and drug solubility in core tablet.[11] Rheumatoid Arthritis (RA) is very frequent occurring disease mostly in elderly people above age of 65 years.[12] RA is chronic inflammatory disorder in joints. However, rheumatoid arthritis affects many parts of the body especially associated with joints pain and stiffness. RA is more commonly found in women.[13] Treatment of RA attempted by various research. Many drugs are available to reduce pain and inflammation, non-steroidal anti-inflammatory medications are very common and frequent. Most of NSAID produces side effect and need to dosing two to three times in a day which is very inconvenient to the patient.[14] Choice of treatment may also affect the patient's other health condition, especially those affecting the GIT, kidney and liver.[15] In treatment of RA, it is important to control the symptoms and joint damage due to inflammation. Among all the RA drugs, Indomethacin is one of the suitable choice for the treatment of RA.[16] It is non-steroidal anti-inflammatory drug regarded as most powerful. Indomethacin is used as benchmark for newer molecule as NSAID.[17] Conventional dosage form of Indomethacin has to be taken two to three times in a day which cause missing of dose and uneven plasma drug concentration that gives side

effect.[18] Hence it needs to make novel drug delivery system of indomethacin. Therefore, it is most suitable candidate with CPOP formulation because this system avoids GIT side effect. Bates T.D., and Kearney M.K., 1987 developed controlled release formulation of indomethacin.[19] The present study was an alternate choice of osmotically controlled release formulation and proved better than EOP.

MATERIAL AND METHODS

Material

Indomethacin was purchased from Sigma Aldrich Pvt Ltd. Other chemical ingredients are Mannitol, Microcrystalline Cellulose, Sodium Chloride, Talc, Magnesium Stearate, Cellulose Acetate, Acetone, HCl, Potassium Dihydrogen Orthophosphate, Disodium hydrogen phosphate, and Potassium Bromide were purchased from Yarrow Chemicals. All are the ingredients were analytical grades. In all the studies there were used doubled distilled water.

Methods

Preparation of the granules of indomethacin by wet granulation method

All the ingredients were accurately weighed, and taken in pestle and mixed uniformly for sufficient time, binder was added in sufficient quantity, then the resulting mixture was passed through sieve of sufficient mesh size, finally the granules were dried in hot air oven.[20]

Preparation of controlled porosity osmotic tablet

CPOP consists of core tablet containing drug and osmogen and other excipients and coated with cellulose acetate solution. Sodium chloride and mannitol was used as a osmogen. The other excipients used in preparation of core tablet include microcrystalline cellulose, magnesium stearate, talc. The prepared core tablet is coated using 4% cellulose acetate in acetone.[21]

Compression Stage

The drug, osmogene, diluent was mixed properly and granules were prepared by wet granulation technique. Magnesium stearate, talc was used as a glidant and lubricant. The formulation was compressed using circular punches and total weight of individual tablet was made to 100mg. The obtained tablets were evaluated for pre-compression and post-compression properties.[22]

Coating Stage

The tablets were coated using standard coating pan. The coating solution is 4% cellulose acetate. 4gm of cellulose acetone was dissolved in 100ml of acetone to form a coating solution. After coating the tablets were evaluated for parameters like hardness, thickness, friability, and weight variation.[23]

CHARACTERIZATION OF INDOMETHACIN GRANULES
(PRE COMPRESSION PROPERTIES).

Bulk density

Weighed accurately 5.00 gm of sample powder and transferred into 50 ml of measuring cylinder, then volume of measuring cylinder was noted by visual observation. Hence mass of powder was recorded previously and volume of powder in measuring cylinder was also noted. Then by using following formula of bulk density was calculated.[24]

Density=Mass/Volume

Tapped density

By tapping 100 times of measuring cylinder filled with powder previously in bulk density measurement. Then volume of tapped measuring cylinder was recorded. Same procedure was performed in triplicate. Following formula was used in calculation of tapped density.[25]

Tapped density = weight of blends/Tapped volume of blends

Hausner's ratio

Hausner ratio is numeric value which was obtained by mathematical calculation of the ratio of tapped density and bulk density. Formula used in obtaining Hausner ratio given as below.[26]

Hausner ratio = Tapped density/poured density.

Carr's index

Carr's index parameter of flow property was determined by taking difference of tapped density and bulk density, then that difference was divided by tapped density and then whole was multiplided by 100 to determine carr's index. Mathematical formula for carr's index was used and given as below.[27]

$$\textbf{Carr's index} = \frac{\textbf{[Tapped density- Bulk density] X 100}}{\textbf{Tapped density}}$$

The correlation between the Carr's index and the flow property of the material was taken by standard table.

Angle of Repose

To determine angle of repose, weighed accurately 5 gm of powder was passed through funnel fixed with stand, the tip of funnel was fixed above 5 cm above from the surface of plane paper. Powder were passed through orifice of funnel which had made pile of powder. A circle was drawn around the pile of powder then height of pile was measured through double scale at touching the scales perpendicularly. Then powder was removed from paper sheet and radius was measured by making squire outside of circle, four sides of squre touched as tangent of circle the diameter was drawn vertically and diagonally. Such that radius of circle determined. Then the values of height of pile and radius of pile were putted in the formula and calculated to determine angle of repose.[28]

$\tan \theta = h/r$

Where θ was angle of repose, r was radious of pile and h was height of the pile.

CHARACTERIZATION OF INDOMETHACIN TABLETS
(POST COMPRESSION PROPERTIES OF TABLETS)

Weight variation

Weight variation of tablet was estimated by 20 tablet weighed accordingly and average weight was determined and compared with individual weight of tablet. As per IP not more than two tablet exceed out of rage of weight variation. Percentage weight variation was determined by putting the values in following formula of weight variation.[29]

$$\%\text{Deviation} = \frac{(\text{Average weight} - \text{Tablet weight}) \times 100}{\text{Average weight}}$$

Hardness

Randomly 3 tablet were selected from each formulation. One tablet was palaced diagnolly between the plunger of Monsanto hardness tester and pressure was applied until tablet broken into two part completely at that point reading was noted down in unit of Kg/cm^2.[30] Procedure was triplicated.

Thickness

Tablet's thickness was measured by Vernier calipers. In which tablet were placed between catcher of the Vernier calipers and a nobe was moved to hold tightly, then it was measured by visual observation.

Drug content of core Tablet

Prepared 10 tablets of Indomethacin were converted into powdered form and weighed equivalent to 25 mg Indomethacin. Powder equivalent to 25 mg indomethacin were added to 10 ml of distilled water and allow to stand for 15 minutes. And then 75 ml of methyl alcohol solution was added in stirring condition then volume made up to 100 ml with sufficient amount of methyl alcohol. Equal volume of buffer solution (pH 7.2) and methyl alcohol added to 5 ml of that solution. Then it was measured at 320 nm by UV Visible spectrophotometer. Drug content was calculated using standard calibration curve indomethacin.

***In-vitro* dissolution study of core tablets**

***In-vitro* drug release study of coated tablets**

Prepared Indomethacin loaded CPOP tablet were subjected to analyze its In-Vitro release in which USP II apparatus in 0.1 HCL buffer at 37 ± 0.5^{O}C at 50 rpm for initial 2 hours after that test were performed in 6.8 phosphate buffer for 4.0 hours then next in 7.4 phosphate buffer for 6 hrs. From each individual time period, a 5 ml of sample was withdrawn and replaced with the fresh buffer and withdrawl sample was filtered and subjected for UV spectrophotometer analysis at 320 nm. For each formulation, the lag time and % release was calculated.

Development of Calibration curves.

Linear plot of Indomethacin in pH 1.2 buffer

A 100 ml volumetric flask was taken and filled with preweighed 50 mg of Indomethcin with Hcl buffer. Solution was obtained as concentration of 500 mcg/ml, from this solution 1 ml was taken and diluted with same 0.1N Hcl buffer solution up to 25 ml as stock solution of 20µg/ml concentration. From stock solution, 1ml, 2ml, 3ml, 4ml, 5ml solution was withdrawn and subsequent dilution were made 2µg/ml, 4µg/ml, 6µg/ml, 8µg/ml and 10µg/ml respectively. These samples were analyzed at 320 nm in UV Visible spectrophotometer to get absorbance and calibration graph was taken. Standard graph of indomethacin was plotted against conc. Vs absorbance.

Solubility Studies

Knowing a drug's aqueous solubility properties is crucial since just a little amount of water solubility is required for it to have therapeutic effects. The medication was dissolved in a constant volume of buffers with pH values of 1.2, 6.8, and 7.4 and the resultant solutions were stored at RT for 24 hours while being periodically shaken. Filtering and drug-dissolve analysis were performed on the resultant solutions using a UV spectrophotometer with a maximum wavelength of 320 nm.

Table 7: Formulation of compressed tablet of indomethacin.

Ingredients in (mg)	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
Indomethacin	50	50	50	50	50	50	50	50	50	50
NaCl	15	-	7.5	35	-	17.5	26.2	8.8	23.3	11.7
Mannitol	-	15	7.5	-	35	17.5	8.8	26.2	11.7	23.3
PVP K-30	6	6	6	6	6	6	6	6	6	6
Magnesium stearate	4	4	4	4	4	4	4	4	4	4
MCC	25	25	25	5	5	5	5	5	15	15

RESULTS AND DISCUSSION

Pre-compression characteristics of pure drug

Prier identification was done by visual examination.

Organoleptic properties: Drug was identified by organoleptic properties such as taste - slightly bitter, colour -White, odour - odourless and description – crystalline shown.

Solubility

The drug was found to be soluble in P^H in pH 6.8 when compared to that of in pH 0.1N HCl buffer and in phosphate buffer pH 7.4.

Standard plot of Indomethacin in 0.1N HCl

The standard equation for indomethacin was found to be y = 0.0061x+0.001 with (R^2= 0.9934). The linearity plot was obtained for the aliquot concentration of 5, 10, 15, 20, 25 µg/ml with absorbance seen at 320 nm.

Table 8: Standard plot of Indomethacin in 0.1N HCl.

Conc. (µg/ml)	Absorbance by UV
0	0
5	0.031
10	0.062
15	0.102
20	0.124
25	0.151

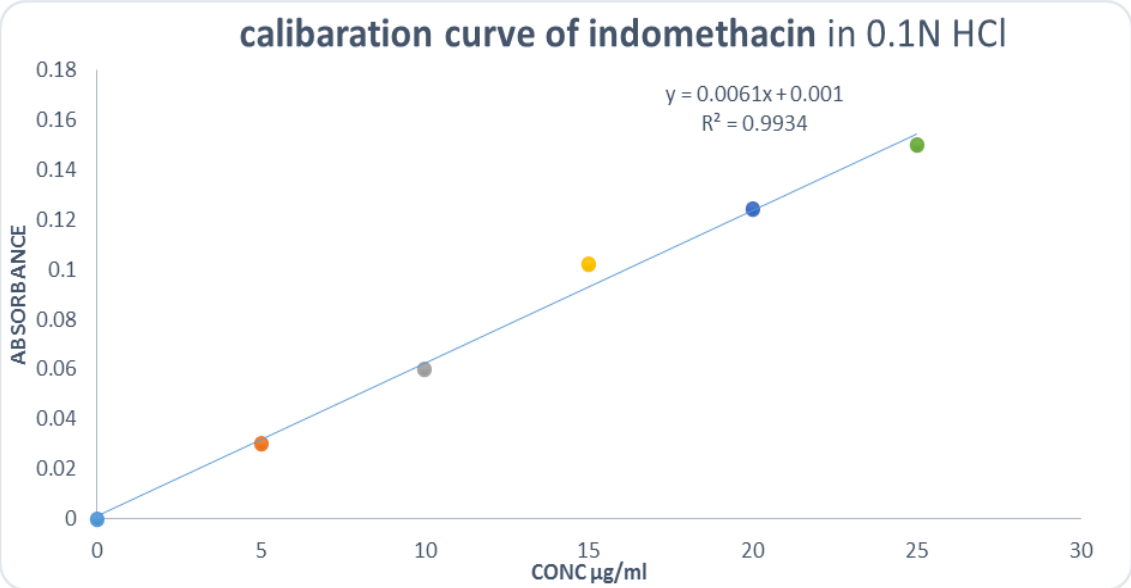

Figure 9: Standard plot of Indomethacin 0.1N HCl.

FTIR STUDIES

The drug-polymer compatibility was assed by I.R spectra of the drug, polymer, and mixture of both. The 0-H stretching frequency of pure drug and polymer was noted at 3372 cm^{-1} and 3110 cm^{-1} respectively. Where as frequency for the same in mixture was showed at 3110 cm^{-1} and 3348 cm^{-1}. Since there is no significant change in 0-H in I.R spectra of sample. It indicates that there is no considerable chemical interaction between the drug and polymers used. The I.R spectra of the compounds are shown below.

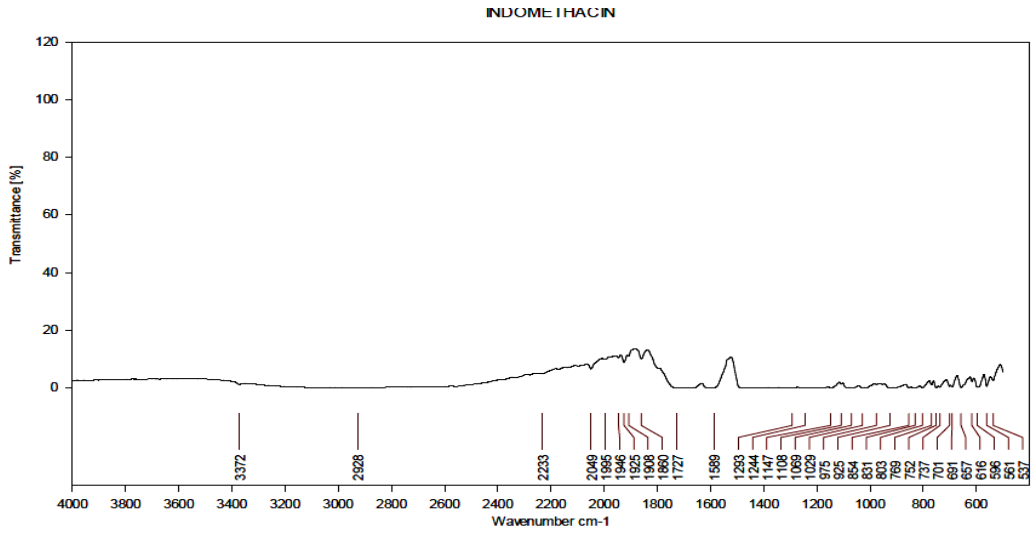

Figure 12: FTIR Studies of Indomethacin.

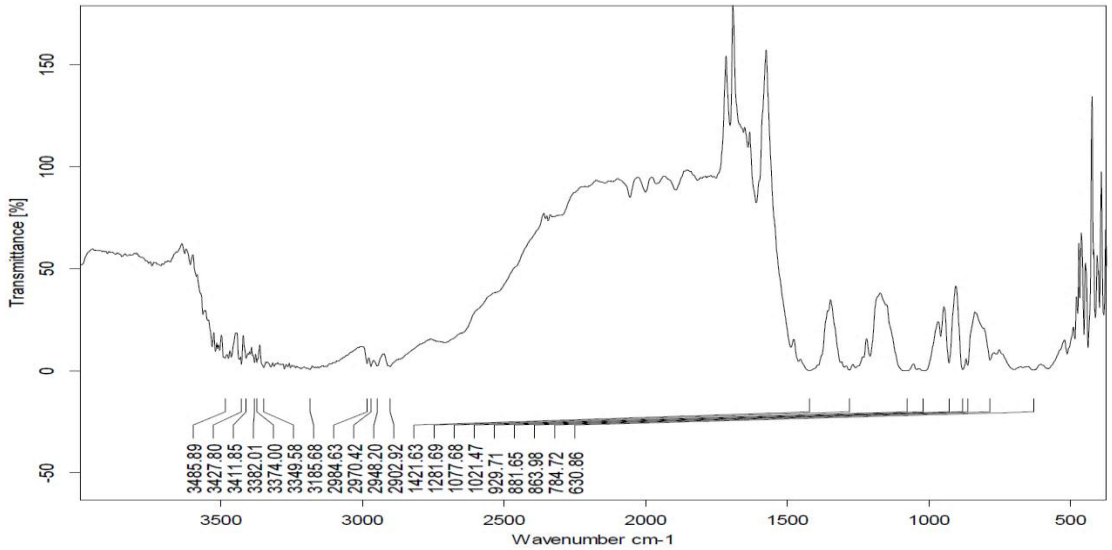

Figure 13: FTIR Studies of mannitol.

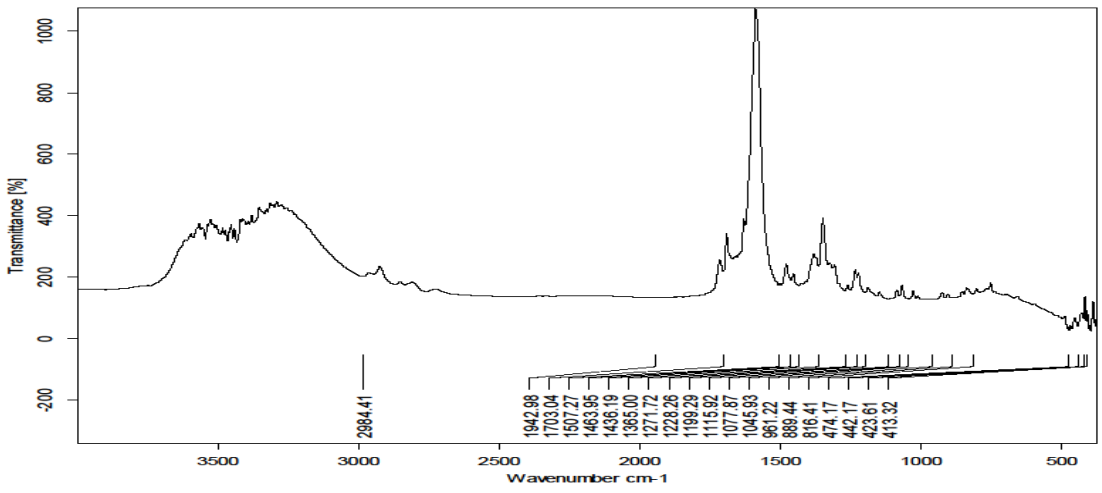

Figure 14: FTIR Studies of Sodium chloride.

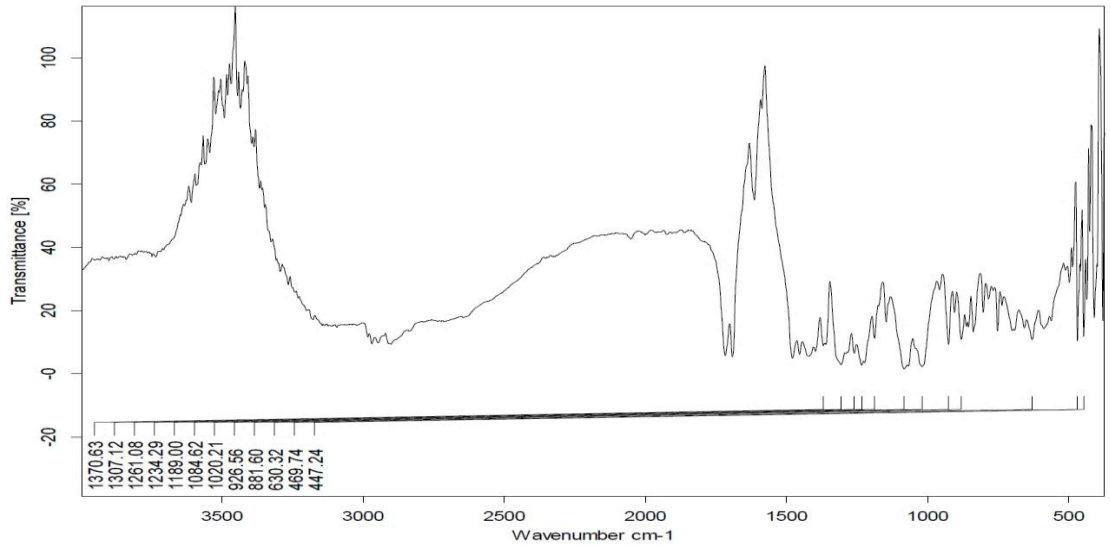

Figure: FTIR studies of Indomethacin and Mannitol.

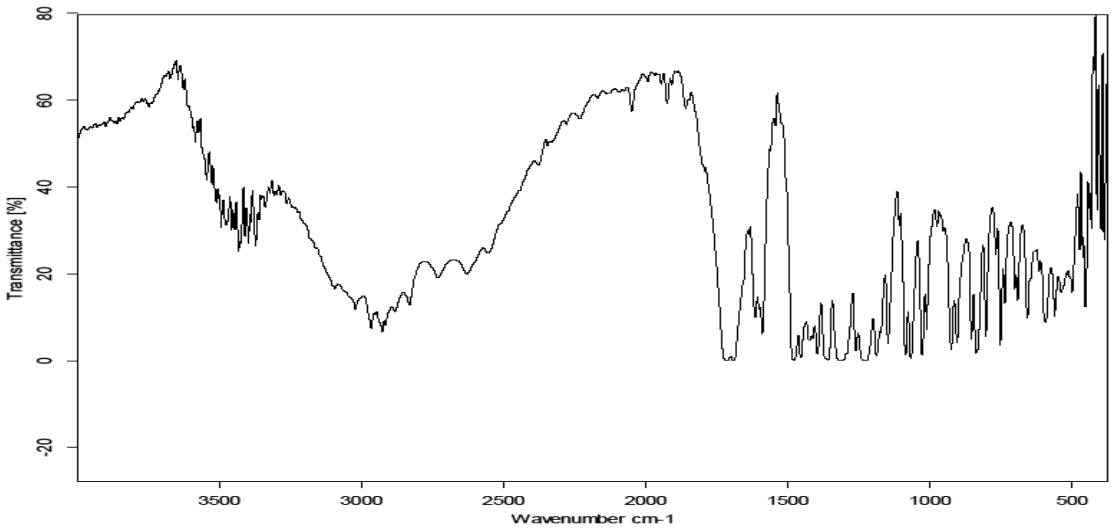

Figure 16: FTIR Studies of Indomethacin and Sodium chloride.

Table 11: Evaluation of The Granules.

Formulations	Bulk Density (g/cm^3)	Tapped Density (g/cm^3)	Carr's Index (%)	Hausner's ratio	Angle of Repose (degrees)
F-1	.625	.714	12.46	1.14	27.30
F-2	.552	.606	8.91	1.09	24.22
F-3	.590	.689	14.3	1.16	27.24
F-4	.520	.606	14.2	1.16	23.74
F-5	.515	.588	12.4	1.14	19.71
F-6	.505	.571	11.5	1.13	20.80
F-7	.588	.714	17.0	1.21	21.30
F-8	.550	.645	14.7	1.17	25.64
F-9	.660	.740	10.8	1.12	27.92
F-10	.600	.667	10.0	1.11	27.33

Evaluation of the granules

Angle of repose is the most important of the several angular parameters that have been used to assess flowability. Investigated was the granules' angle of repose. Angle of repose (0°) values dropped after lubricant was added. An indicator of powder flowability from the hopper to the die cavity during the compression of tablets is the angle of repose (0°). All of the formulations had an angle of repose between 200 and 300, which is a sign of high flowability. Based on the size, shape, and propensity of particles to stick together, bulk density can affect a number of qualities, including compressibility, tablets' porosity, dissolving, and other features. Granules were discovered to have a bulk density of 0.51 to 0.62 gm/cm3. The results show that the packing capacity of granules. The granules' tapped density was discovered to be between 0.58 and 0.74 gm/cm3. The % compressibility of the granules was calculated using the bulk density and tap density.

The granules' Carr's index was found to be in the 8.90 to 17.0 range, showing strong compressibility. Indicating good flowability, the values of the Hausner's ratio were determined to be in the range of 1.09 to 1.21.

Table 12: Evaluation of The Core Tablet.

Formulations	Thickness (mm)	Weight variation (%)	Hardness (Kg/Cm^3)	Friability (%)	Drug Content
F-1	2.52	PASSED	5.8	.72%	94.6%
F-2	2.62	PASSED	5.2	.68%	93.8%
F-3	2.45	PASSED	4.8	.81%	97.8%
F-4	2.42	PASSED	5.0	.93%	100.6%
F-5	2.50	PASSED	7.1	.49%	96.5%
F-6	2.52	PASSED	6.2	.50%	98.4%
F-7	2.47	PASSED	6.3	.48%	106.5%
F-8	2.51	PASSED	5.4	.78%	95.8%
F-9	2.61	PASSED	4.9	.98%	98.4%
F-10	2.49	PASSED	6.8	.50%	103.4%

Evaluation of core tablet

***Surface morphology of tablets*:** The surface of the tablets was found to be smooth and uniform. There was no indication of non-uniformity of coating.

Thickness: The thickness of the tablet was found out using vernier caliper and thickness of core tablet was found to be in range of 2.42 to 2.62mm.

***Weight variation test*:** The uniformity of weights was determined according to IP specifications and the variation in weight of tablets were found to be within the limit (>5%). Hence all the formulations (F1-F10) passed the test.

Hardness: The hardness of the tablets were measured by Monsanto hardness tester. Ten core tablets from the batch were used for hardness studies and result showed they were in the range between 4.8 to 7.1 kg/cm^2.

The hardness was found to be in the range of IP specification.

Drug content analysis: Indomethacin controlled release controlled porosity tablet was tested as per USP for drug content and all formulations showed drug content in the range of 93.8% to 106.5%.

EVALUATION OF THE COATED TABLET

Weight gained by the coated tablets: An increase in the weight of tablets were observed after coating of the compressed coat tablet. The percentage increase in the weight of the tablet were found to be within the range of 3% to 5%.

Table 13: Post compression result of prepared formulations.

Formulations	Weight variation (%)	Hardness (Kg/Cm^3)	Weight gain by coated tablet
F-1	Passed	6.1	2.9%
F-2	Passed	5.8	3.8%
F-3	Passed	5.4	3.03%
F-4	Passed	5.6	3.06%
F-5	Passed	7.5	3.92%
F-6	Passed	6.3	3.12%
F-7	Passed	6.9	4.2%
F-8	Passed	5.7	2.97%
F-9	Passed	5.4	3.84%
F-10	Passed	7.4	2.94%

Hardness: A significant increase in the hardness of the tablet was exhibited by all the formulations. The average increase of .45Kg/cm2 in hardness of the tablets was observed due to cellulose acetate coating.

Weight variation test: The uniformity of weights was determined according to IP specifications and the variation in weight of tablets were found to be within the limit (>5%). Hence all the formulations (F1-F10) passed the test.

Dissolution Study

Osmotic tablet were subjected to *in-vitro* drug release studies in simulated gastric and intestinal fluid. Dissolution study was performed in 0.1N HCL for 1st and 2nd hour and for next 4 hours in phosphate buffer 6.8 and remaining period in phosphate buffer 7.2.

From the data it is evident that increase in the concentration of osmogen caused increase in the drug release from the system. Pore forming agent (PEG400) produces s significant effect on release profile.

Dissolution profile reveals that drug release from the system was more in 0.1N HCL.

Table 14: In vitro dissolution profile of formulation F1 to F5.

Time (Hr)	Dissolution media	Cumulative percentage release of drug (%)				
		F1	F2	F3	F4	F5
1	0.1 N HCL	8.7	7.6	9.6	8.5	11.06
2		11.2	12.6	17.3	19.3	18.3
3	pH 6.8 phosphate buffer.	17.4	16.2	19.4	29.4	21.9
4		21.3	19.3	23.1	32.1	27.6
5		29.6	23.1	27.5	44.7	36.1
6		37.3	27.5	36.9	58.4	39.2
7	pH 7.2 phosphate buffer.	41.2	36.2	39.6	69.2	46.1
8		47.3	41.3	47.4	78.1	53.2
9		68.4	45.2	51.2	86.2	58.6
10		77.9	48.3	57.6	98.4	69.3
11		89.6	56.2	62.5		76.2
12		97.8	60.9	66.6		84.1

Table 15: In vitro dissolution profile of formulation F6 to F10.

Time (Hr)	Dissolution media	Cumulative percentage release of drug (%)				
		F6	F7	F8	F9	F10
1	0.1 N HCL	11.2	7.3	6.3	9.2	8.3
2		19.4	13.4	11.4	16.1	13.6
3	pH 6.8 phosphate buffer.	25.2	28.4	19.2	18.6	16.36
4		31.6	37.2	27.1	23.2	21.31
5		37.2	46.1	36.1	34.1	27.62
6		44.2	58.2	39.2	38.2	31.21
7	pH 7.2 phosphate buffer.	59.2	66.1	44.6	43.9	37.1
8		67.2	76.2	56.1	53.2	43.2
9		73.1	89.4	67.2	60.21	45.1
10		79.4	93.2	71.3	62.36	49.2
11		87.1	96.8	81.1	67.31	53.2
12		93.2		83.7	72.11	59.6

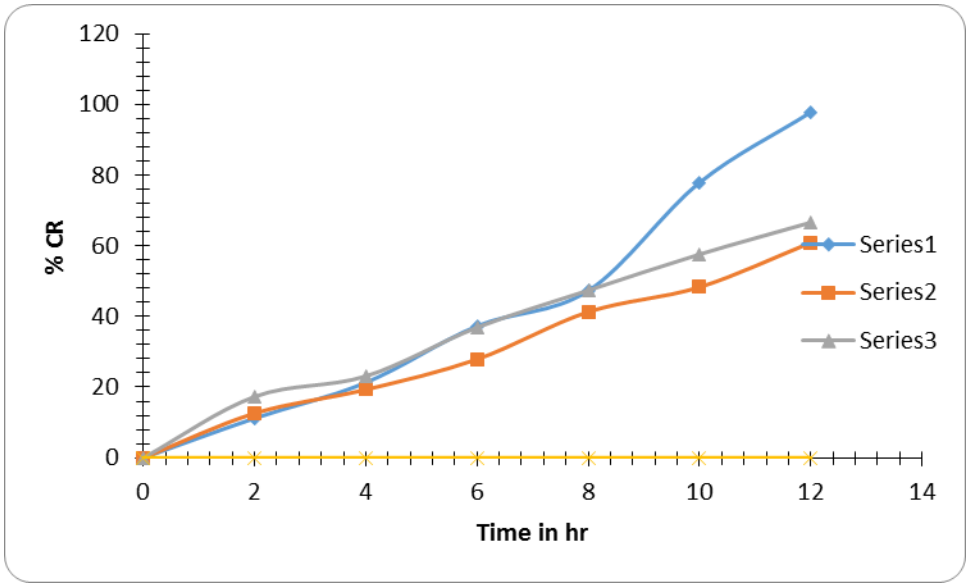

Figure 17: Dissolution profile of various formulations (F1 to F3).

The dissolution profile indicates after 3 hours the formulation F1, F2, F3 releases 25.2, 28.2 and 19.2% of the drug respectively. This is mainly due to type of osmotic agent used.

At the end of 12 hr the formulation F1 released 93.2%, F2 released 96.8% and F3 released 83.7%.

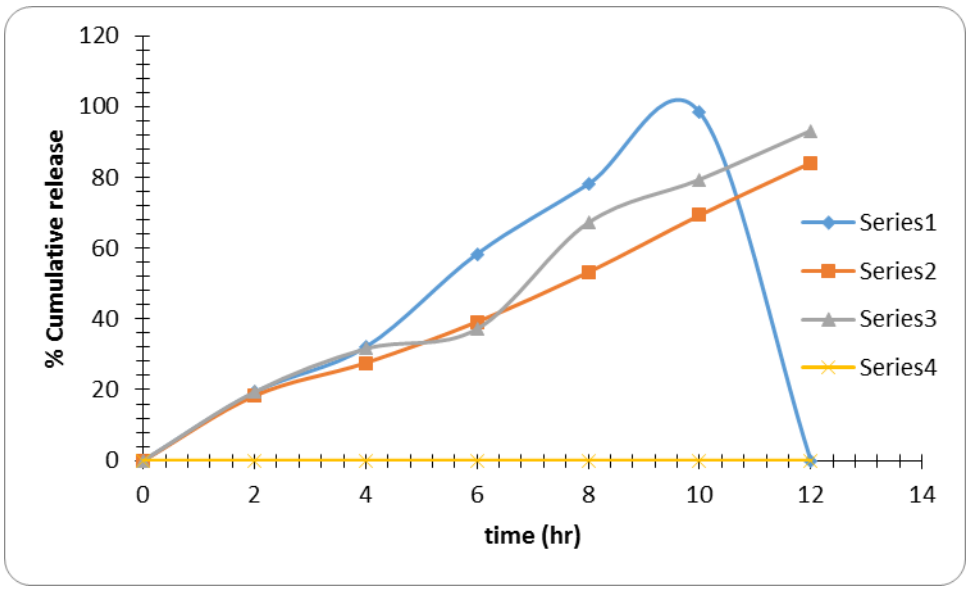

Figure 18: Dissolution profile of various formulations (F4 to F6)

From the dissolution study formulation F4, F5 and F6 showed 29.4, 21.9 and 25.2% drug release after 3 hours, the highest release was shown by F4 due to high amount of NaCl as osmogen.

At the end of 12 hours the release were 98.4, 84.1 and 93.2%, at the end of 12 hr F4 showed complete drug release.

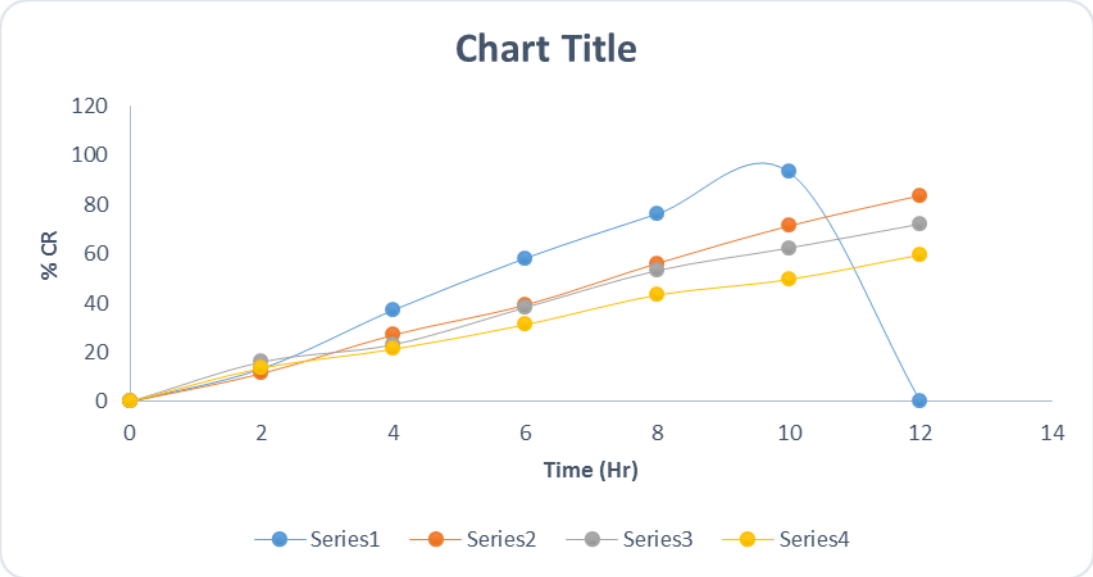

Figure 19: Dissolution profile of various formulations (F7 to F10)

The dissolution profile indicates that after 3 hr the formulation F7, F8, F9, F10 releases 28.4, 19.2, 18.6, 16.36% drug release. As the concentration of osmotic agent increases percent drug release also increases. At the end of 12 hr the release rate were 96.8, 83.7, 72.11 and 59.6% respectively. F7 showed complete release while F10 showed 59.6% release.

Table 16: Release Kinetics.

S.No	Time (Hr)	Log Time	Square Root Of Time	%Cumulative Drug Release	Log Cumulative Drug Release
1	0	0	0	0	0
2	2	.3010	1.414	19.4	1.2878
3	4	.6020	2.000	31.6	1.4996
4	6	.7781	2.449	44.2	1.6454
5	7	.8450	2.646	59.2	1.7723
6	8	.9630	2.828	67.2	1.8273
7	10	1	3.162	79.4	1.8998
8	12	1.0791	3.464	93.2	1.9694

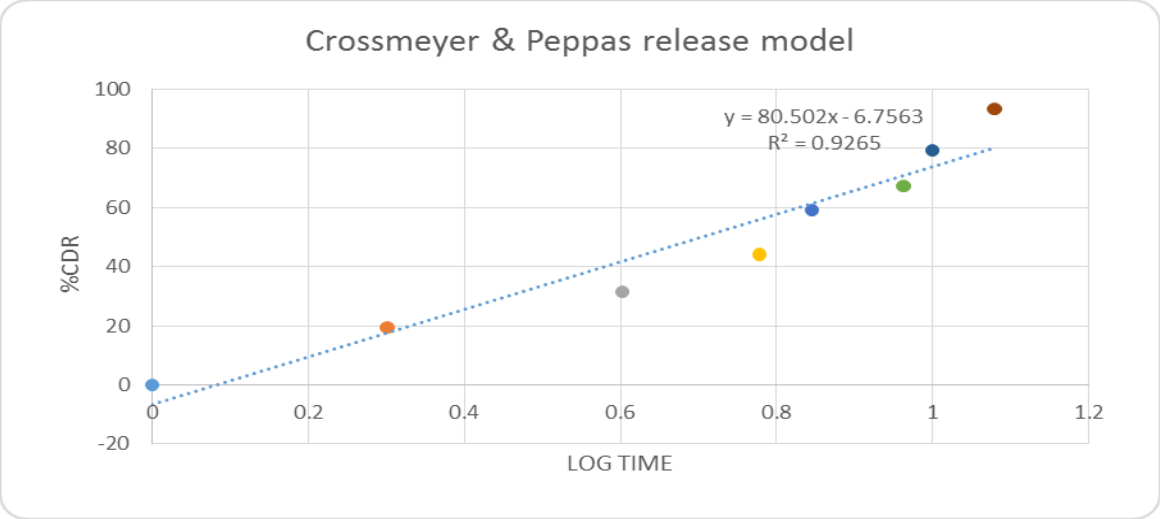

Figure 20: Korsmeyer and Peppas release model.

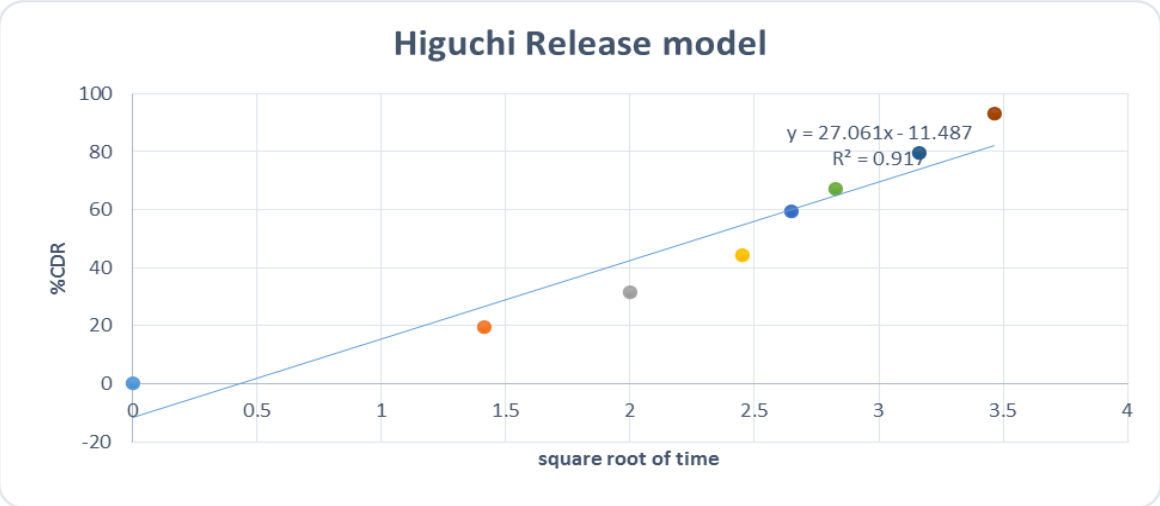

Figure 21: Higuchi release model.

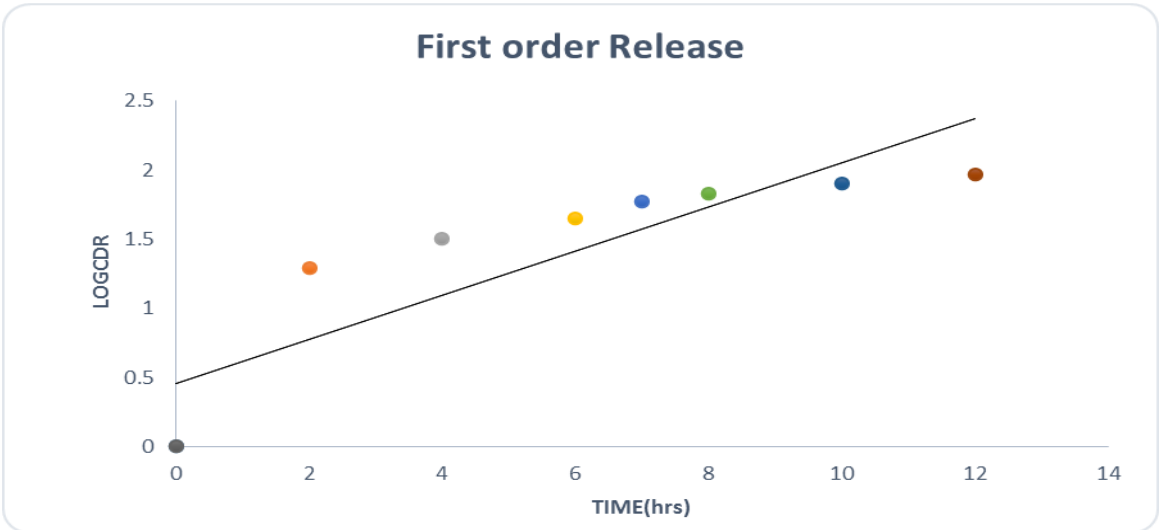

Figure 22: First Order release model.

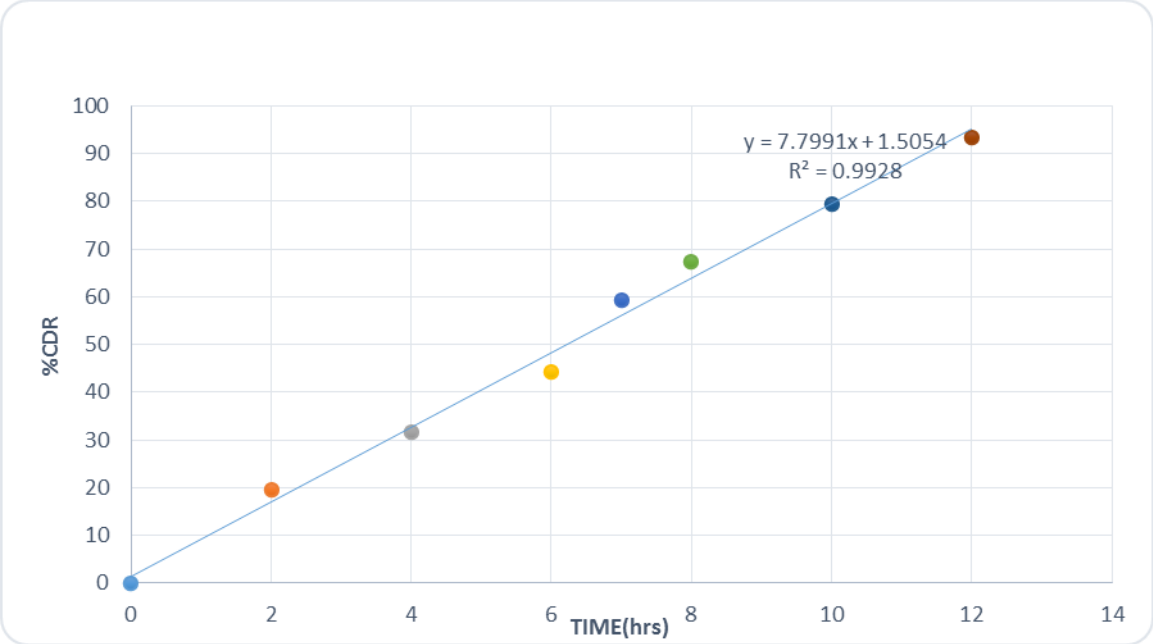

Figure 23: Zero Order release model.

Comparative study of EOP and Marketed SR Product

The comparative study of dissolution profile of EOP Tablets of indomethacin with marketed sustained release product indicated that F11 showed a controlled release of drug up to 12 hours where as marketed SR dosage form taken to study released all the drug in 10 hours. Hence EOP tablets with is considered to be more reliable than the matrix SR dosage form.

Table 17: Study of EOP and Marketed SR Product.

S.no	Time(hrs)	Cumulative Percentrage drug release(%) SR Formulation	Cumulative Percentrage drug release(%) EOP Formulation	
			0.6mm Orifice	0.7mm Orifice
1.	0	0	0	0
2.	2	51.2	8.69	10.87
3.	4	79.0	20.64	22.48
4.	6	88.0	46.42	52.58
5.	8	93.4	66.2	76.39
6.	10	102.1	86.46	89.1
7.	12	102.1	96.2	98.24

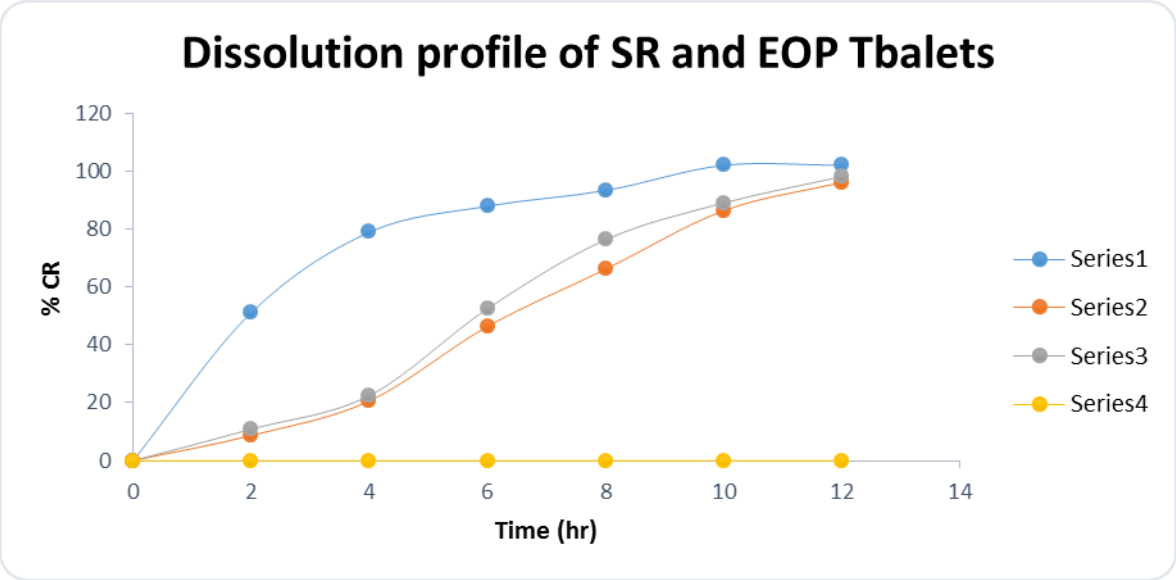

Figure 24: Dissolution profile of SR and EOP tablets.

CONCLUSION

Oral dosage form accounts for the largest proportion of administered pharmaceuticals. Osmotically regulated oral drug delivery system is suitable for the controlled release of the drug throught the GI tract. In the present study the controlled porosity osmotic tablet for indomethacin was developed. The controlled porosity osmotic drug delivery system consists of the core tablet containing drug and osmogens along with other excipients and finally coated with polymer mixed with pore forming agent which is water soluble in nature. The formulation leads indicated controlled release of indomethacin, avoided dose dumping and extended duration of action. Membrane were found to develop pores/channel after coming in contact with aquous environment due to the dissolving of the water soluble pore former. The comparative study carried out between the marketed SR product and EOP clearly indicated that EOP is ideal for delivery of indomethacin for about 12 hours whereas the marketed SR product released maximum drug in 10 hours. The comparision of release profile of EOP with CPOP (F1-F10) indicates that the CPOP is suitable for delivery of indomethacin for more than 12 hours. It can be concluded that CPOP is ideal for the delivery of the drug where release of the drug is required to be for more than 12 hours. The CPOP is cost effective technology along with reduced dosing frequency and increased patient compliance.

REFERENCES

1. Shokri J, Ahmadi P, Rashidi P, Shahsavari M, Rajabi-Siahboomi A, Nokhodchi A. Swellable elementary osmotic pump (seop): An effective device for delivery of poorly water-soluble drugs. Eur J PharmBiopharm, 2008; 68: 289-97.
2. Makhija SN, Vavia PR. Controlled porosity osmotic pump-based controlled release system of pseudoephedrine-I cellulose acetate as a semipermeable membrane. J Control Release, 2003; 89: 5-18.
3. Verma RK, Kaushal AM, Garg S. Development and evaluation of extended release formulations of isosorbide mononitrate based on osmotic technology. Int J Pharm, 2003; 263: 9-24.
4. Rao BP, Geetha M, Purushothama N, Sanki U. Optimization and development of swellable controlled porosity osmotic pump tablet for theophylline. Trop J Pharm Res, 2009; 8: 247-55.
5. Verma RK, Mishra B, Garg S. Osmotically controlled oral drug delivery. Drug Dev Ind Pharm, 2000; 26: 695‑708.
6. Thombre AG, Appelb LE, Chidlaw MB, Daugherity PD, Evans LA, Sutton SC. Osmotic drug delivery using swellable-core technology. J Control Release, 2004; 94: 75-89.
7. Zenter GM, Rork GS, Himmelstein KJ. The controlled porosity osmotic pump. J Control Release, 1985; 1: 269-82.
8. Li X, Jasti BR. Osmotic controlled drug delivery systems. In: Design of controlled release of drug delivery systems. McGraw Hill New York, 2006; p. 203‑29.
9. Babu CA, Rao MP, Ratna V. Controlled-porosity osmotic pump tabletsan overview. J Pharm Res Health Care, 2010; 2: 114-26.
10. Pan H, Jing H, Yang X, Pan W, Chen T. Synchronized and controlled release of metformin hydrochloride/glipizide from elementary osmotic delivery. Drug Dev Ind Pharm, 2017 May; 43(5): 780-788. doi: 10.1080/03639045.2016.1200071. Epub 2016 Jun 29. PMID: 27278057.
11. Conley R, Gupta SK, Sathyan G. Clinical spectrum of the osmotic-controlled release oral delivery system (OROS*), an advanced oral delivery form. Current Medical Research and Opinion®, 2006; 22(10): 1879-92.
12. Feinglos M, Dailey G, Cefalu W, et al. Effect on glycemic control of the addition of 2.5 mg glipizide GITS to metformin in patients with T2DM ☆. Diabetes Res Clin Pract, 2005; 68(2): 167-75.

13. Gupta BP, Thakur N, Jain NP, et al. Osmotically controlled drug delivery system with associated drugs. J Pharm Pharm Sci, 2010; 13(4): 571-88.
14. Chen J, Pan H, Ye T, et al. Recent aspect of osmotic pump system: functionalization, clinical use and advanced imaging technology. Current Drug Metabolism, 2015; 75(2): 183-6.
15. Malaterre V, Ogorka J, Loggia N, et al. Oral osmotically driven systems: 30 years of development and clinical use. Eur J Pharm Biopharm, 2009; 73(3): 311-23.
16. Bird, H. A., (1986). Drug therapy for arthritis. Practitioner, 230: 323-330.
17. Capell, H. A., (1986). Rheumatoid arthritis. Practitioner, 230: 353-356.
18. Capell, H. A., Daymond, J. T.., and Dick, W. C., (1983). Pharmacology of the drugs used in the treatment of chronic arthritis. In: "Rheumatic Disease", p 129. Ed.: J. L. Reid. Springer Verlag, Berlin.
19. Pullar, T., Mayall, 0. Haigh. J. R., Lowe, J. R., Dixon, J. S., and Bird, H. A., (1988). The effect of indomethacin on the psychomotor function of patients with rheumatic diseases. 61J:. Rheumatol, 27: 227-229.
20. Huskisson, E. C., (1979). Routine drug treatment of rheumatoid arthritis and other rheumatic diseases. Ciiri. Rheum. Dis, 5: 697-706.
21. Bates, T. D., and Kearney, M. K., (1987). Longer-term control of pain in terminal cancer with MST Continus tablets. In: "1986 International Symposium on Pain Control", pp 5-12. Ed.: D. Doyle. Symp. Ser. No. 123. Royal Society of Medicine Services, London.