IJPSR (2013), Vol. 4, Issue 8 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 22 March, 2013; received in revised form, 08 May, 2013; accepted, 21 July, 2013; published 01 August, 2013

FORMULATION AND CHARACTERIZATION OF CONTROLLED POROSITY OSMOTIC TABLETS OF ACYCLOVIR FOR TREATMENT OF HERPES SIMPLEX

Anu Kaushal*, Sanjay Jain, Hemant Khambete and Devendra Patidar

Department of Pharmaceutics, Smriti College of Pharmaceutical Education, Indore - 452010, Madhya Pradesh, India

Keywords:

Acyclovir, Scanning electron microscopy, Optimization

Correspondence to Author:

Anu Kaushal

Assistant Professor, Department of Pharmaceutics, Smriti College of Pharmaceutical Education, 4/1 Pipliya Kumar Kakkad, Mayakhedi Road, Indore - 452010, Madhya Pradesh, India

E-mail : anukaushal7@gmail.com

ABSTRACT: The main objective of present work was to formulate and evaluate swellable controlled porosity osmotic tablets of Acyclovir for the treatment of herpes simplex. This formulation aims to release the drug in zero order pattern, increase bioavailability, reduce frequency of drug dosing and hence increased patient compliance. Acyclovir is a synthetic purine nucleoside analogue that is specially activated by Herpes Simplex Virus (HSV) induced thymidine kinase, and inhibits viral DNA polymerases as well as acting as a chain terminator. The technique used for the preparation of tablets was direct compression followed by deep coating of core tablets and total nine formulations (F1-F9) were prepared. Prior to compression, the prepared granules were evaluated for flow and compression characteristics. Prepared osmotic drug delivery system was also evaluated for *in vitro* drug release study. *In vitro* release profile of all formulations was in range from 54.12-99.85%. The formulation F2 was best amongst all and showed 56.58% drug release in 12 hr and 98.92% in 24 hrs. Zero order drug release kinetics was shown by formulation F2 at 0-24 hr which is require for enhance bioavailability of acyclovir. Further, among coated formulations (C1-C8), C7 showed sufficient strength and formed smooth surface. The coating did not show any leakage and was stable during dissolution of tablet. The % weight gain of coated tablet was found to be in range 1.98-2.40%. The thickness of semipermeable membrane was 240 µm and membrane withstands the pressure during the dissolution. The surface morphology of the coating membrane was examined using Scanning Electron Microscopy after dissolution and showing pore formation in membrane. Accelerated stability studies were conducted for optimized formulation as per specified ICH guidelines for one month. Formulations were found to be stable for one month when tested for drug content as well as *in vitro* dissolution studies.

INTRODUCTION: Conventional drug delivery systems have little or no control over the drug release, and effective concentration at the target site. This kind of dosing pattern may result in constantly changing, unpredictable plasma concentrations.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.4(8).2955-62

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.4(8).2955-62

Conventional preparation is usually administered two or three times a day, which leads to large fluctuation in drug plasma concentration and side effects on human body. Constant plasma level, can offer a therapeutic advantage for many drugs in terms of both efficacy and tolerance of the treatment. Once-daily controlled release preparation is often desirable [1-3].

Development of oral controlled release dosage forms of a given drug involves optimization of the dosage form characteristics within the inherited constraints of the gastrointestinal physiology.

Controlled release delivery systems have added advantages over immediate release dosage form. These include reduction of dosing frequency by administering the drug once or twice a day. Since the frequency of drug administration is reduced, patient compliance can be improved, and drug administration can be more convenient due to reduction of gastrointestinal side effects. These also cause less fluctuations of plasma drug level and lead to more uniform drug effect and lesser total dose [4-6].

Various techniques have been used in the formulation of controlled release products. In general, controlled release formulations can be divided into different categories based on the mechanism of drug release [7]. A number of design options are available to control or modulate the drug release from a dosage form. Osmotically controlled oral drug delivery systems are those which utilize osmotic pressure for controlled delivery of active agent(s).

Drug delivery from these systems, to a large extent, is independent of the physiological factors of the gastrointestinal tract and these systems can be utilized for systemic as well as targeted drug delivery of drugs. The release of drug(s) from osmotic systems is governed by various formulation factors such as solubility and osmotic pressure of the core component(s), size of the delivery orifice, and nature of the rate-controlling membrane. By optimizing formulation and processing factors, it is possible to develop osmotic systems to deliver drugs of diverse nature at a pre-programmed rate [8].

Acyclovir is a synthetic purine nucleoside analogue with *in vitro* and *in vivo* inhibitory activity against human herpes viruses, including herpes simplex virus (HSV) types 1 and 2 Varicella zoster virus (VZV), Epstein Barr virus (EBV) and Cytomegalovirus. The inhibitory activity of acyclovir for HSV 1 and HSV 2, VZV, EBV and CMV is highly selective. The enzyme thymidine kinase (TK) of normal, non-infected cells does not use acyclovir effectively as a substrate, hence toxicity to mammalian host cells is low; however, TK encoded by HSV, VZV and EBV converts acyclovir to acyclovir monophosphate, a nucleoside analogue which is further converted to the diphosphate and finally to the triphosphate by cellular enzymes. Acyclovir triphosphate interferes with the viral DNA polymerase and inhibits viral DNA replication with resultant chain termination following its incorporation into the viral DNA [9].

Thus, there is a strong clinical need and market potential for a dosage form that will deliver acyclovir in a controlled manner to a, thereby resulting in a better patient compliance. The present study was aimed towards the development of controlled release formulations of acyclovir based on osmotic technology.

Different formulation variables were studied and optimized to achieve the desired release profile. The manufacturing procedure was standardized and the stability of the formulation was evaluated after one month of storage at accelerated stability conditions.

MATERIALS AND METHODS

Materials: Acyclovir was obtained as gift sample from Acrolab, Bangalore. Hydroxypropyl methyl cellulose LV 50 (HPMC LV 50), sodium lauryl sulphate (SLS), microcrystalline cellulose (MCC) Polyethylene glycol 400 (PEG 400), Sorbitol, dibutylphthalate, potassium chloride, Cellulose acetate and Potassium dihydrogen orthophosphate were purchased from Loba chem HCl and disodium hydrogen phosphates were purchased from Merck specialties Ltd. Mumbai.

Methods:

Formulation of Acyclovir Core Tablet: The core tablets of acyclovir were prepared by direct compression method using varied concentrations of osmogen (potassium chloride) and polymer Hydroxypropyl methyl cellulose LV 50 (HPMC LV 50). The drug and excipient were passed through sieve no.40. All ingredients were mixed in pestle mortar.

Magnesium stearate and talc were passed through sieve no. 80 mixed and blend with initial mixture. The powder blend was compressed into rotary tablet punching machine. The ingredients with their function are enlisted in **table 1** and the composition of the core tablet formulation is enlisted in **table 2**.

TABLE 1: FORMULATION DESIGN OF CORE TABLET

S. No	Name of Ingredient	Function of Ingredient
1	Acyclovir	Active pharmaceutical ingredient
2	Microcrystalline cellulose	Binder/polymer
3	Hydroxypropyl methyl cellulose	polymer
4	Potassium chloride	Osmogent
5	Sodium lauryl sulphate	Wicking agent
6	Magnesium Stearate	lubricant
7	Talc	Glidant

TABLE 2: COMPOSITION OF CORE TABLET FORMULATION

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Drug	200	200	200	200	200	200	200	200	200
Microcrystalline cellulose	100	100	100	100	100	100	100	100	100
Hydroxy Propyl Methyl Cellulose	75	75	75	100	100	100	150	150	150
Potassium Chloride	50	100	150	50	100	150	50	100	150
Sodium Lauryl Sulfate	25	25	25	25	25	25	25	25	25
Magnesium Stearate	20	20	20	20	20	20	20	20	20
Talc	10	10	10	10	10	10	10	10	10
Total Weight	480	530	580	505	555	605	555	605	655

All the weight expressed in mg

Coating of Acyclovir Core Osmotic Tablet: The coating solution was prepared by dissolving 2 gm Cellulose acetate in 100ml Acetone, Isopropyl alcohol and 2% w/v solution of cellulose acetate was prepared. The plasticizer (dibutylphthalate) and flux regulator (PEG 400) were added in solution. Finally pore forming agent (Sorbitol) was added and solution was stirred for 15 min.

Coating Method: The Tablets were warmed in an oven for 15 min at 45±0.5ºC and were further used for coating. Tablet coating was applied using a dip-coating process/pan coating. The tablets were dip coated in polymer solutions consisting of cellulose acetate dissolved in a mixture of acetone and isopropyl alcohol containing pore forming agent and plasticizer. After coating, the tablets were dried over night at 40ºC to remove residual solvent. The ingredients with their function are enlisted in **table 3** and composition of coating formulation is enlisted in **table 4**.

TABLE 3: FORMULATION DESIGN OF THE COATING OF TABLET

S. No.	Name of Ingredient	Function of Ingredient
1	Cellulose Acetate	Semipermeable Agent
2	PEG 400	Flux Regulator
3	Dibutylphthalate	Plasticizer
4	Sorbitol	Pore Forming Agent
5	Acetone	Coating Solvent
6	Isopropylalcohol	Coating Cosolvent

TABLE 4: COMPOSITION OF COATING FORMULATION

Formulation Code	PEG 400 (ml)	Sorbitol (mg)	Dibutylphthalate (ml)
C1	0.350	0.6	0.8
C2	0.350	0.6	1.4
C3	0.350	1.2	0.8
C4	0.350	1.2	1.4
C5	0.700	0.6	1.4
C6	0.700	0.6	0.8
C7	0.700	1.2	1.4
C8	0.700	1.2	0.8

Characterization:

A. **Evaluation of Granules:** Flow properties of granules were evaluated by established methods [10]. Angle of Repose was determined using funnel method. Bulk Density and Tapped Density and Compressibility Index were calculated.
B. **Evaluation of Core Tablets** [11]: The formulated core tablets were evaluated for different parameters like general characteristic, hardness, thickness and drug content uniformity of tablet.

General Characteristic: General appearance of tablet, its visual identity size, shape, color of tablet was evaluated.

1. **Thickness:** The thickness of the tablets was determined using a digital Vernier calliper. Six tablets from each batch were used, and average values were calculated. The Thickness should be controlled within ±5% variation of a standard value.

2. **Weight Variation Test:** 20 tablets of each formulation were weighed using an electronic balance and the test was performed according to the official method (Indian Pharmacopoeia, 1996). The test was run by weighing 20 tablets individually, calculating the average weight, and comparing the individual tablet weights to the average.

3. **Hardness:** For each formulation, the hardness of 5 tablets was determined using Monsanto hardness tester. The hardness was measured in terms of kg/cm^2.

4. **Friability:** Six tablets were weighed collectively and placed in the chamber of the friabilator. After 100 rotations, the tablets were taken out from the friabilator and intact tablets were again weighed collectively.

$$\text{Friability} = \frac{\text{Initial}_{wt} - \text{Final}_{wt}}{\text{Initial}_{wt}}$$

5. **Uniformity of Drug Content:** Uniformity of drug content was determined by taking 5 tablets in a glass mortar and powdered; 100 mg of this drug powder dissolved in 100 ml 0.1N HCl. The drug was extracted with vigorous shaking and filter and further appropriate dilution were made and absorbance was measured at 253 nm by UV spectrophotometer. [12]

C. **Evaluation of Coated Tablet:** The coated tablets were evaluated for different parameters like visual identity, weight gain of core tablet, thickness of membrane and surface morphology of membrane.

1. **Measurement of Film Thickness:** Following the completion of dissolution, the film was isolated from the tablets and dried at 40^oC for 1 hr. Thickness was measured at three different points on the film using electronic digital callipers and the mean values were taken.

2. **Scanning Electron Microscopy:** The surface morphology of the optimized tablet film coating after dissolution was examined by scanning electron microscope. Prior to examination sample were mounted on an aluminum stub using a double sided adhesive tape and then making it electrically conductive by coating with a thin layer of gold in vacuum at an acceleration voltage of 20 kv.12

3. ***In-vitro* Release Studies:** *In vitro* drug release of the formulations was carried out in a USP dissolution apparatus (paddle type) set at a rotating speed of 50 rpm and temperature of 37 ± 1^oC. The dissolution medium (900 ml) was 0.1N HCl for the first 2 h and phosphate buffer (pH 6.8) thereafter. Samples (5 ml) were withdrawn at specified time intervals over a 24 h period and the medium was replenished with fresh dissolution fluid. The samples were diluted to 10 ml and assayed for drug content spectrophotometrically at 253 nm [13].

RESULTS AND DISCUSSION:

Drug-Excipients Interaction Studies: The IR spectra for drug and physical mixture with drug were obtained using FTIR instrument. The FT-IR spectra of pure drug and its physical mixture were taken for the interaction studies.. This observation clearly suggests that the drug remains in its normal form with no prominent interaction occur in drug and excipients. **Figure 1** shows comparison between drug and physical mixture [14].

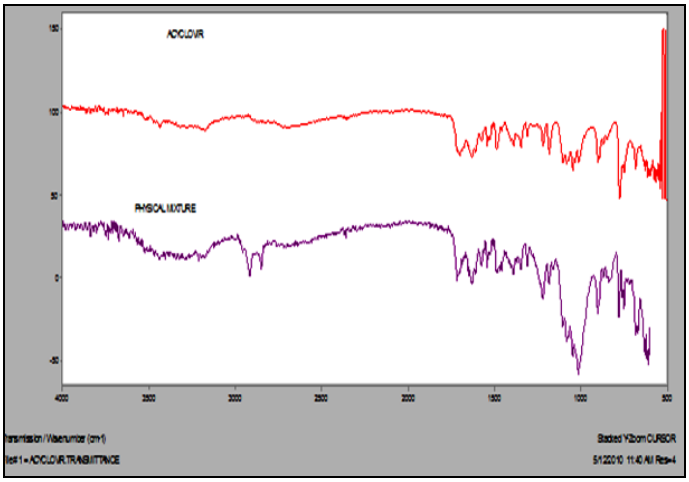

FIGURE 1: COMPARISON OF FTIR PEAKS OF DRUG AND PHYSICAL MIXTURE OF DRUG

Micromeritic Evaluation: The micromeritic properties of powder blend is shown in **Table 5**. The powder showed improved flowability, good compressibility of powder as observed from the values of angle of repose (25.21–28.18 0) and Compressibility Index (15.2-21.8%) respectively [15].

General Characteristic: The core tablets were white, circular, smooth surface and concave in shape.

Thickness: Thickness was found to be in range of 5.396-5.776 mm which was found to be satisfactory.

Hardness: The hardness was found to be in range 5.3-6.1 kg/cm^2 which were found to be satisfactory for direct compression.

Friability: Friability of all batches was in range of 0.45 to 0.61% which is in accordance to IP limit of less than 1%. This was found to be satisfactory.

Weight Variation: Mean of weight variation of twenty tablets from each formulation were taken and found to be in accordance with IP.

Uniformity of Content: Uniformity of drug content of all batches was in range of 98.96 to 99.74% which was within the acceptable limits.

TABLE 5: MICROMERITICS OF POWDER

Formulation Code	Angle of Repose	Bulk Density	Tapped Density	Compressibility Index (%)	Flowability
F1	27.284±1.363	0.510±0.012	0.621±0.013	17.8±0.03	Good
F2	27.321±1.221	0.529±0.025	0.627±0.006	15.6±0.04	Good
F3	28.146±1.007	0.568±0.015	0.670±0.012	15.2±0.02	Good
F4	25.218±1.126	0.462±0.023	0.572±0.021	19.2±0.05	Good
F5	28.182±1.096	0.480±0.013	0.592±0.015	18.9±0.04	Good
F6	26.701±1.165	0.501±0.014	0.633±0.012	20.80±0.02	Good
F7	26.629±1.136	0.380±0.024	0.486±0.014	21.8±0.05	Good
F8	26.129±1.432	0.398±0.017	0.502±0.017	20.7±0.05	Good
F9	27.216±1.086	0.416±0.023	0.518±0.012	19.6±0.04	Good

All the value are express as mean ±S.D, n=3

TABLE 6: POST COMPRESSION PROPERTIES OF CORE TABLET

Formulation Code	Property				
	Average weight (mg)*	Thickness (mm)n	Hardness (kg/cm^2)n	Friability (%) #	Uniformity of Content (%)n
F1	474±7.1	5.336±0.012	6.1±0.4	0.453±0.03	99.10
F2	530±6.8	5.501±0.015	5.9±0.3	0.487±0.02	98.96
F3	574±7.6	5.561±0.011	5.6±0.2	0.543±0.03	99.41
F4	505±6.5	5.425±0.012	6±0.3	0.469±0.02	99.31
F5	545±7.4	5.537±0.009	5.8±0.2	0.520±0.03	99.23
F6	596±8	5.572±0.011	5.5±0.2	0.557±0.04	99.74
F7	551±7.3	5.545±0.008	5.7±0.3	0.527±0.02	99.63
F8	597±7.8	5.568±0.017	5.5±0.2	0.569±0.04	99.58
F9	674±8.1	5.776±0.014	5.3±0.1	0.610±0.05	99.15

All the value are expressed as mean ±S.D, n=3,*=20, # =6

Coated Tablet: Out of total coating formulations, C7 has sufficient strength and smooth surface. The coating did not show any leakage and was stable during dissolution of tablet. **The table 7** shows the data of percentage weight gain of coated tablet.

TABLE 7: PERCENTAGE WEIGHT GAIN OF CORE TABLET COATED

Formula	Property			
	No. of Tablets	Core tablet weight (mg)	Weight of coated tablet	% weight gain
F1	1	475	486	2.30
	2	468	481	2.40
F2	1	531	544	2.40
	2	528	540	2.20
F3	1	575	588	2.21
	2	581	595	2.22
F4	1	512	524	2.34
	2	505	517	2.37
F5	1	551	563	2.17
	2	545	557	2.20
F6	1	601	613	1.99
	2	604	616	1.98
F7	1	554	565	1.98
	2	547	558	2.01
F8	1	601	614	2.16
	2	605	618	2.14
F9	1	654	668	2.14
	2	653	667	1.99

***In-vitro* Dissolution Study:** Dissolution study was carried out on all formulations using USP apparatus in 900 ml of 0.1N HCl (pH 1.2) for the first two hrs and then using PBS (pH 6.8) maintained at 37±0.5^{o}C at a speed of 50 rpm. Samples of dissolution medium were withdrawn after regular time intervals and were replaced with equal volume of fresh medium. The samples were filtered and analyzed for drug release by measuring the absorbance at 253 nm after suitable dilution with 0.1 HCl and phosphate buffer (pH 6.8). The comparative percentage cumulative drug release shows that the formulation F2 shows optimum drug release at required time duration among all the formulations. Dissolution data of coated tablets is shown in **figure 2 and table 8** shows dissolution release profile of all formulations. Formulation F2 showed drug release at 24 hr and regression factor is 0.991. **Table 9** shows regression data of all formulations.

TABLE 8: DISSOLUTION RELEASE PROFILE OF OSMOTIC TABLET

Time (hr)	% Cumulative Drug Release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
1	2.12±0.30	5.61±0.33	7.42±0.23	1.50±0.09	2.70±0.13	3.54±0.10	1.10±0.12	2.01±0.16	2.7±0.19
2	3.39±0.18	10.03±0.24	12.14±0.32	3.21±0.18	5.54±0.19	6.96±0.19	2.72±0.18	4.24±0.15	6.3±0.18
3	6.57±0.16	14.12±0.28	16.54±0.41	6.01±0.20	8.64±0.23	13.17±0.23	5.56±0.21	6.64±0.20	11.04±0.28
4	9.06±0.09	17.82±0.19	23.87±0.28	8.89±0.16	11.42±0.21	18.85±0.26	8.06±0.26	9.93±0.31	14.52±0.28
5	11.77±0.32	23.49±0.26	30.35±0.33	10.78±0.21	14.70±0.31	24.94±0.33	10.07±0.19	13.20±0.21	17.82±0.24
6	14.54±0.28	29.08±0.21	36.39±0.54	14.03±0.55	19.23±0.25	31.46±0.41	13.13±0.25	16.24±0.28	21.07±0.32
7	17.39±0.17	32.98±0.32	42.77±0.61	16.57±0.31	22.97±0.34	37.89±0.28	15.57±0.52	19.24±0.33	24.57±0.41
8	20.17±0.41	38.25±0.25	48.67±0.48	18.64±0.24	27.04±0.33	44.43±0.39	17.63±0.35	21.97±0.43	28.27±0.29
9	23.21±0.34	42.86±0.31	54.97±0.55	21.10±0.35	29.84±0.42	49.27±0.35	19.66±0.37	24.66±0.39	33.06±0.25
10	25.29±0.33	47.41±0.43	61.30±0.43	23.17±0.26	34.15±0.53	55.26±0.47	21.38±0.51	28.02±0.41	39.01±0.38
11	28.17±0.23	51.14±0.25	66.62±0.40	26.32±0.42	37.97±0.33	58.06±0.58	27.26±0.51	31.24±0.43	43.17±0.28
12	31.24±0.28	56.58±0.16	71.35±0.26	30.54±0.33	41.97±0.47	63.36±0.46	29.01±0.37	34.24±0.43	47.40±0.54
13	37.32±0.43	37.32±0.43	77.55±0.35	34.41±0.61	46.17±0.42	67.23±0.67	32.52±0.28	36.70±0.36	52.17±0.44
14	40.38±0.15	65.12±0.33	81.55±0.42	38.23±0.49	50.52±0.39	71.06±0.46	36.12±0.33	39.58±0.45	56.51±0.36
24	60.49±0.30	98.92±0.28	99.85±0.48	58.81±0.56	80.10±0.56	95.15±0.57	54.12±0.53	65.80±0.39	90.62±0.48

All the value are expressed as mean ±S.D, n=3

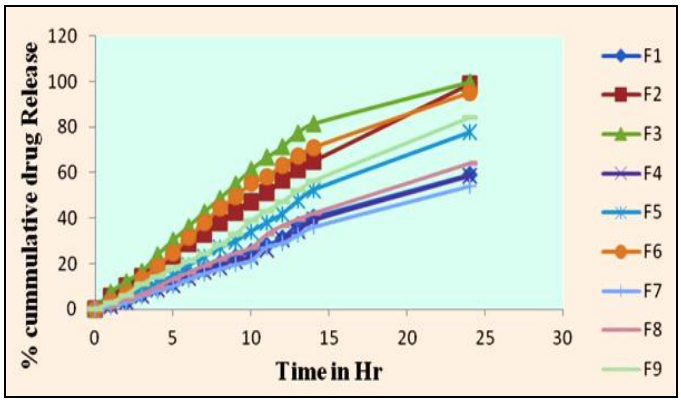

FIGURE 2: PERCENTAGE CUMULATIVE DRUG RELEASE OF DIFFERENT FORMULATION

Thickness of Film: After completion of dissolution, the film was isolated from the tablets and dried at 40°C for 1 hr. the thickness of semipermeable membrane was 240 µm and membrane withstand the Pressure during the dissolution. **Figure 3** shows the coating thickness.

Scanning Electron Microscopy: The surface morphology of the coating membrane was examined using Scanning Electron microscopy after dissolution. The SEM Result showing smooth surface membrane and pore formation in membrane is shown in **Figure 4** [16].

TABLE 9: REGRESSION FACTOR OF DIFFERENT FORMULATION

	Formulation								
r2	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
	0.988	0.991	0.930	0.990	0.990	0.950	0.988	0.980	0.989

FIGURE 3: LAYER OF COATING AFTER DISSOLUTION

Stability Study of Optimized Formulation (F2+C7): The prepared tablets were evaluated for Hardness, Weight variation, Thickness, film thickness, uniform weight gain and *in vitro* release profile. Overall results indicate that formulation F2+C7 is the better in all preparation and satisfies all the criteria as an osmotic tablet.

The accelerated stability study of optimized formulation was performed as per ICH (International Conference of Harmonization) guidelines at 40°C and 75% RH for one month. The results of stability studies in **table 10** reveal that general appearance, hardness, content of active ingredient all the parameter were in acceptable range.

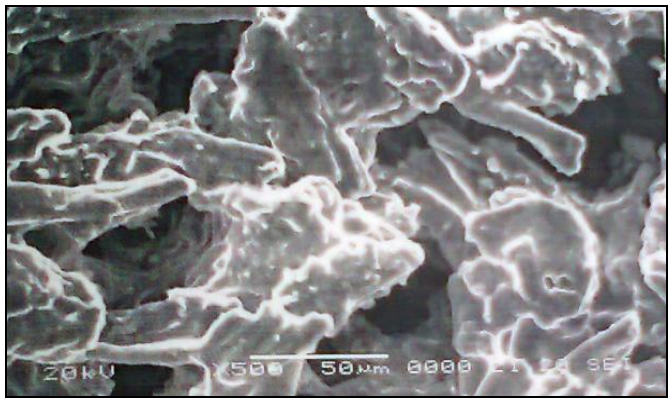

FIGURE 4: SEM MICROPHOTOGRAPH OF MEMBRANE, SHOWING FORMATION OF PORES

TABLE 10: STABILITY STUDY OF OPTIMIZED BATCH OF OSMOTIC TABLET

Parameters	**Time**		
	0 day	**15 days**	**30 days**
Physical appearance	White	White	White
Weight (mg)	542.1±0.92	542.6±0.94	543.1±0.94
Hardness (kg/cm^2)	5.9±0.038	5.7±0.026	5.7±0.023
% Drug content	98.96±0.06	98.93±0.06	98.93±0.06

*All values are expressed as mean ±SD (n=6)

CONCLUSION: In the present work, swellable controlled porosity osmotic tablet of acyclovir was successfully formulated by direct compression technique. Out of total nine formulations the formulation F2 showed the best results as compared to other batches.

The formulation F2 showed 56.58% drug release at 12 hr and 98.92 drug releases at 24 hr and coating formulation C7 has sufficient strength and form smooth surface. The coating was not leakage and stable during dissolution of tablet. % weight gain of coated tablet and comply with the requirements for controlled release formulations.

ACKNOWLEDGEMENT: The authors are thankful to Acrolab, Bangalore, for providing facilities to carry out the Research work.

REFERENCES:

1. HC Ansel, LV Allen and CG Popovich: In Pharmaceutical dosage form and drug delivery system. B.I. Wavery Pvt. Ltd. New Delhi. 2000; 66:60-61.
2. T Ghosh and A Ghosh: Drug delivery through osmotic systems. J App pharma sci. 2011; 2: 38-49.
3. Robinson JR(Ed): Sustained and controlled release drug delivery system. Marcel Dekker. New York. Second ed; 1980: p.no 213.
4. G Zentner, Rork and K Himmelstein: The controlled porosity osmotic pump. J Cont Release. 1985; 1:269-282.
5. R Baker: Controlled release delivery system by an osmotic bursting mechanism.US patent.1987; 3,952,741.
6. S Vyas, Khar RK: Controlled Drug Delivery Concepts and Advances. 3th ed. Vallabh Prakashan 2005; P: 412-446.
7. Theeuwes: Microporous-semipermeable laminated osmotic system.US Patent.1978; 4,256,108.
8. K Okimoto, Rajewski, Stella V: Release of testosterone from an osmotic pump tablet utilizing (SBE) -b-cyclodextrin as both a solubilizing and an osmotic 7m pump agent. J Controlled Release. 1999; 58: 29–38.
9. K D Tripathi: Essential of medical pharmacology.2008; 6th edition New delhi
10. Jaypee brother medical publication (P) Ltd.P:769-79. Leon Lachman, Liberman, Kanig JL: The theory and practice of industrial pharmacy. 3rd ed., Varghese publishing house.1987; 171-196.
11. SH Lakade, M Bhalekar: Formulation and Evaluation of Sustained Release Matrix Tablets of Anti-Anginal drug, Influence of combination of hydrophobic and hydrophilic matix former. Research J. Pharm. and Tech. Jan – Mar 2008; 1: 410-413.
12. Indian Pharmacopoeia. Vol. II, Ghaziabad: Indian Pharmacopoeia Publication, 1996.
13. Mohd Azharuddin, Krishnananda Kamath, T. Panneerselvam, Subash S. Pillai, A.R. Shabaraya: Formulation and evaluation of controlled release matrix tablets of antihypertensive drug using natural and synthetic hydrophilic polymers. Research in Biotechnology 2011; 2: 26-32.
14. A Choudhury, S Das, S Bahadur, S Saha, A Roy: Formulation and evaluation of omeprazole tablets for duodenal ulcer. Indian Journal of Pharmaceutical Sciences 2010; 72: 491-494.
15. Dinanath Gaikwad, Jadhav RT, Amol Limkar, Sangeeta, Kisan Bobe, Manoj Patil, Trushali Khade, Bhaskar Gavitre, Vivek Kulkarni, Uday Gaikwad: Formulation and Evaluation of Sustained Release Tablet of Aceclofenac by Film Coating. International Journal of Research in Pharmaceutical and Biomedical Sciences Jan – Mar 2011; 2: 310-318.
16. A. Uma Maheswari*, K. Elango, Daisy Chellakumari, K. Saravanan and Anglina Jeniffer Samy: Formulation and evaluation of controlled porosity osmotic tablets of lornoxicam. International Journal of Pharmaceutical Sciences and Research. 2012; Vol. 3, Issue 06.1625-1631.

How to cite this article:
Kaushal A, Jain S, Khambete H and Patidar D: Formulation and characterization of Controlled Porosity Osmotic Tablets of Acyclovir for treatment of Herpes Simplex. *Int J Pharm Sci Res* 2013: 4(8); 2955-2962. doi: 10.13040/IJPSR. 0975-8232.4(8).2955-62