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FORMULATION AND EVALUATION OF *SWELLABLE CONTROLLED POROSITY* OSMOTIC PUMP TABLET OF THEOPHYLLINE

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Abstract: **Objective:** Formulation and Evaluation of osmotic pump tablets of Theophylline. **Experimental Work:** A swellable controlled porosity osmotic pump based drug delivery system has been described in this study. Controlled porosity of the membrane is accomplished by the use of channeling agent. The usual dose of Theophylline was 150 mg to be taken once a daily. The plasma half life of Theophylline was 8 h. Hence, Theophylline was chosen as a model drug with an aim to develop a controlled release system for 24 h. Sodium chloride was used as osmogent. Cellulose acetate was used as the semi permeable membrane. The porous osmotic pump contains pore forming water-soluble additive (Poly ethylene glycol 400) in the coating membrane which after coming in contact with water, dissolve, resulting in an in situ formation of micro porous structure. The effect of different formulation variables, namely, ratio of drug to osmogent, membrane weight gain and concentration of pore former on the in vitro release was studied using 23 full factorial design. The effect of pH and agitation intensity on drug release was also studied. The optimized formulation was subjected to stability study for one month period. **Results:** It was found that drug release rate increased with the amount of osmogent because of increased water uptake, and hence increased driving force for drug release. Drug release was inversely proportional to membrane weight gain: however, directly related to the concentration of pore former in the membrane. A surface plot is also presented to graphically represent the effect of independent variables on t_{90}. **Conclusion:** Optimized formulation was found to release above 90% of drug (Theophylline) at a zero order rate for 24 h.

Keywords: Semi permeable membrane, Osmogent, Plasticizer, Hydrogel Polymer, Full factorial design.

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INTRODUCTION

CONTROLLED POROSITY OSMOTIC PUMP TABLET

During the past three decades significant advances have been made in the area of the novel drug delivery. In a typical therapeutic regimen the drug dose and dosing interval are optimized to maintain drug concentration within the therapeutic window, thus ensuring efficacy while minimizing toxic effects. Survey indicated that dosing more than one or twice daily, greatly reduces patient compliance. So in recent year considerable attention has been focused on the development of novel drug delivery system and the main reason for this paradigm shift is relatively low development cost and time required for introducing a novel drug delivery system as compared to a new chemical entity. In the form of novel drug delivery system, an existing drug molecule can get a new life there by increasing its market value competitiveness and patent life among the various novel drug delivery system available in the market, per oral controlled release system hold the major market share because of their obvious advantages of ease of administration and better patient compliance. These products provide significant benefits over immediate release formulation, including greater effectiveness in the treatment of chronic conditions, reduced side effects, and greater patient convenience due to simplified dosing schedule.[2]

A number of design options are available to control or modulate the drug release from a dosage form. Majority of per oral dosage form fall in the category of matrix, reservoir or osmotic system. In matrix system, the drug is embedded in polymer matrix and the release takes place by partitioning of drug into the polymer matrix and the release medium. In contrast, reservoir systems have a drug core coated by the rate controlling membrane. However factor like pH, presence of food and other physiological factor may affect drug release from conventional controlled release systems. Osmotic systems utilize the principle of osmotic pressure for the delivery of drugs. Drug release from these systems is independent of pH and other physiological parameter to a large extent and it is possible to modulate the release characteristic by optimizing the properties of drug and system.[1]

The bioavailability of drug from these formulations may vary significantly, depending on factors such as physicochemical properties of the drug, presence of excipients, various physiological factors such as the presence or absence of food, pH of the GI tract and GI motility. To overcome this limitation of oral route is replied by parenteral route. This route offers the advantage of reduced dose, targeting of site and avoiding GI stability, hepatic by-pass of drug molecule.

In the recent years, pharmaceutical research has led to the development of several novel drug delivery systems. The role of drug development is to take a therapeutically effective molecule with sub-optimal physiological properties and develop an optimized product that will still

be therapeutically effective but with additional benefits such as, greater effectiveness in the treatment of chronic conditions, sustained and consistent blood levels within the therapeutic window, enhanced bioavailability, reduced inter patient variability, customized delivery profiles, decreased dosing frequency, improved patient compliance due to simplified dosing schedule, reduced side effects.[5]

The controlled porosity osmotic pump tablet is a spray coated or coated tablet with a semi-permeable membrane containing leachable pore forming agents. They do not have any aperture to release the drugs; drug release is achieved through the pores, which are formed in the semi permeable wall *in situ* during the operation. In this system, the drug, after dissolution inside the core, is released from the osmotic pump tablet by hydrostatic pressure and diffusion through pores created by the dissolution of pore formers incorporated in the membrane. The hydrostatic pressure is created either by an osmotic agent or by the drug itself or by a tablet component, after water is imbibed across the semi permeable membrane. This membrane after formation of pores becomes permeable for both water and solutes. A controlled porosity osmotic wall can be described as having a sponge like appearance. The pores can be continuous that have micro porous lamina, interconnected through tortuous paths of regular and irregular shapes. Generally, materials (in a concentration range of 5% to 95%) producing pores with a pore size from 10 Å -100 µm can be used[3].

Fig 1: Controlled porosity osmotic pump

This system is generally applicable for only water-soluble drugs as poorly water soluble drugs cannot dissolve adequately in the volume of water drawn into the osmotic pump tablet. Recently this problem was overcome by adding agents like sulfobutyl ether-β-cyclodextrin (SBE) 7m-β-CD or Hydroxypropyl-β-cyclodextrin (HP-β-CD) as solubilizing and osmotic agents. Several approaches have been developed to prepare the porous membrane by spray coating using polymer solutions containing dissolved or suspended water-soluble materials. The rate of drug release can also be varied by having different amounts of osmogents in the system to form different concentrations of channeling agents for delivery of the drug from the device. Incorporation of the cyclodextrin-drug complex has also been used as an approach for delivery of poorly water-soluble drugs from the osmotic systems, especially controlled porosity osmotic pump tablets[7].

Advantages

• The controlled porosity osmotic pump tablets can be so designed that delivery of its drug would follow zero order kinetics and thus better control over the drug's *in vivo* performance is possible.

• The drug release from the osmotically controlled drug delivery systems are independent of the gastric pH and hydrodynamic conditions, which is mainly attributed to the unique properties of the semi permeable membrane employed in the coating of osmotic formulations.

• The delivery rate of drug from these systems is highly predictable and can be programmed by modulating the terms.

• It is possible to attain better release rates than those obtained with conventional diffusion based drug delivery systems.

• Drug release from the osmotic drug delivery system exhibits significant *in vitro-in vivo* correlation within specific limits.

Basic components required for controlled porosity osmotic pump[5,8,13]

A. Drug selection criteria

B. Osmotic agent[8]

C. Semi permeable membrane[5]

D. Channeling agents or pore forming agents[13]

MATERIALS

Tab 1: List of materials used in formulation of osmotic pump tablet

Sr. No.	Materials	Source
1	Theophylline	Cadila pharmaceuticals
2	Isubgul Husk	Sulab chemicals, Baroda
3	Sodium Chloride	ACME chemicals, Bombay
4	Micro Crystelline Cellulose	ACME chemicals, Bombay
5	Lactose	S.D.fine chemical, Bombay

6	Starch	ACME chemicals, Bombay
7	Magnesium stearate	S.D.fine chemical, Bombay
8	Talc	S.D.fine chemical, Bombay
9	Cellulose Acetate	Corel pharmachem, Ahmadabad
10	Polyethylene Glycol 400	S.D.fine chemical, Bombay
11	Acetone	ACME chemicals, Bombay

METHODS

ANALYTICAL ESTIMATION OF DRUG

Determination of UV absorption maxima (λ_{max})[45]

10mg of Theophylline was accurately weighed and transferred to 100ml of volumetric flask. The drug was dissolved in water and the volume was made up to 100ml (0.1N HCl, phosphate buffer 6.8 and phosphate buffer 7.4) to obtain a stock solution of 100µg/ml. Two ml of this stock solution was again diluted with dissolution media (0.1N HCl, phosphate buffer 6.8 and phosphate buffer 7.4) up to 10ml to obtain a solution of 20µg/ml. The resulting solution was scanned between 200nm to 400nm in a double beam UV- visible spectrophotometer (shimadzu 1800).

Preparation of 0.1N hydrochloric acid[55]

Measure accurately 8.5 ml of concentrated hydrochloric acid using 10 ml pipette. Dilute it up to 1000 ml with distilled water in 1000 ml volumetric flask.

Preparation of phosphate buffer pH 6.8[55]

Measure accurately 250 ml of 0.2 M monobasic potassium phosphate solution and 112 ml of 0.2 M sodium hydroxide solution was mixed in 1000 ml of volumetric flask and volume was made to 1000 ml with distilled water.

Preparation of phosphate buffer pH 7.4[55]

Measure accurately 250 ml of 0.2 M monobasic potassium phosphate solution and 195.5 ml of 0.2 M sodium hydroxide solution was mixed in 1000 ml of volumetric flask and volume was made to 1000 ml with distilled water.

Preparation of calibration curve

Preparation of stock solution of Theophylline in phosphate buffer pH 7.4

10mg of Theophylline was accurately weighed and transferred to 10ml of volumetric flask. The drug was dissolved in phosphate buffer pH 7.4 and the volume was made up to 10ml to obtain a stock solution of 1000µg/ml (stock solution I). One ml of this stock solution was again diluted with phosphate buffer pH 7.4 up to 10ml to obtain a solution of 100µg/ml (stock solution II).From stock solution II aliquots of 0.2, 0.4, 0.6, 0.8 & 1.0ml were transferred to a series of 10ml volumetric flasks. The volume was made up with phosphate buffer pH 7.4 fluid to give 2, 4, 6, 8, 10 µg/ml of concentration. The absorbance of these solutions was measured at 269.32nm against blank.

Preparation of core tablet[57]

Core tablets of Theophylline were prepared by wet granulation method. All the ingredients were passed through sieve # 60 separately, weighed and mixed in geometrical order. Then bimd with 10 %w/v starch paste, then pass through # seive 60, put them for drying for 30 min at 65˚c. Then dry granuls passed from # seive 120, lubricant and glidant (standard sieve # 120) were added and mixed for further 5 minute. The resulting powder mixtures were then compressed into tablets using a rotary tablet machine fitted with 10 mm flat faced punches.

PREPARATION OF COATING SOLUTION[57]

Selection of polymer

In controlled porosity osmotic pump tablet, required semi permeable membrane as a film former. Cellulose acetate is insoluble in water (excellent solubility in organic solvent), independent of the pH and agitation (physiological condition). So, controlled release can be easily achieved by using this polymer. It is one of the most suitable membranes due to its mechanical strength, semi permeable property and generally regarded as safe polymer. The permeability can be adjusted modifying pore former levels and/or altering membrane thickness. While other polymers like ethyl cellulose, eudragit RL or eudragit RS are pH independent. Eudragit RS or eudragit RL films are very flexible, have a high strain and breaks upon puncture with small cracks. In contrast, ethyl cellulose films are more brittle with a lower strain and complete film rupture is noticed. Hence they were not selected as a polymer.

Selection of pore former

PEG 400 was selected as pore former, because it is hydrophilic material. So, forming pores in coating film. It has plasticizer property. It is best suited with cellulose acetate as pore former. It was used on the basis of % w/w of coating polymer.

Selection of solvents

Solvent were selected based on solubility of both polymers (cellulose acetate) and plasticizer PEG 400. Both are soluble in acetone and hence this was selected as a solvent for coating solution.

Preparation of polymeric coating solution

Coating solution was prepared by mixing 4% w/v of cellulose acetate (semi permeable membrane) and 10%, 20%, 30% w/w PEG 400 (pore former and plasticizer) in acetone and stirred on magnetic stirrer to get homogeneous coating solution.

Dip coating method[57]

In the present study, dip coating method was used to coat the tablets. The formulation A was used as the core tablets. The weighed core tablets were dipped into coating solutions by holding with forceps and after dipping were placed on a glass plate (smeared with PEG 400) for drying in air for 15 minutes at room temperature. The tablets were then dried at 60°C in an oven for 30 minutes. During drying, the tablets were rotated occasionally. The tablets were subjected to coat about 5 %w/w, 8 %w/w and 10 %w/w of total weight of tablet.

Tab 2: Composition of factorial design formulation

Ingredients (mg)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
Theophylline	150	150	150	150	150	150	150	150
Isubgul husk	25	25	25	25	25	25	25	25
NaCl	150	150	150	150	200	200	200	200
MCC	50	50	50	50	30	30	30	30
Lactose	65	65	65	65	35	35	35	35
Mg-stearate	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5

Talc	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5
Starch paste	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Coating								
Cellulose acetate (%w/v)	4 gm	4 gm	4 gm	4 gm	4 gm	4 gm	4 gm	4 gm
PEG 400 (%w/w)	10	10	20	20	10	10	20	20
Acetone	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Weight gain (%w/w)	8	10	8	10	8	10	8	10

In vitro drug release study of factorial design formulations

In vitro release of theophylline from factorial design formulations was carried out by using USP type II apparatus for 24 h at a rotation speed of 50 rpm and at 37 ± 0.5°C using 900 ml phosphate buffer pH 7.4. At appropriate time intervals, dissolution samples were withdrawn and filtered. Samples were analyzed at 270 nm by using UV-visible double beam spectrophotometer.

RESULTS

EVALUATION OF CORE TABLETS

Pre compression parameters of core tablet

The results of angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio indicates that powder blend has good flow property with good compressibility and suitable for direct compression method. The results of powder bland of formulation A to C are shown in Table 3.

Post compression parameters of core tablet

The mean value of friability, thickness, weight and content uniformity of prepared core tablets of Theophylline are shown in Table 5.6. Tablets prepared by wet granulation technique showed uniform thickness, diameter and acceptable weight variations limit as per

pharmacopoeial specifications. Hardness was found in the range of 5 to 5.5 kg/cm^2 for all the formulations of the core tablet and the friability for all formulations was found to be less than 1% indicating sufficient mechanical integrity and strength of the prepared tablets. The results of powder bland of formulation A to C are shown in Table 4.

Tab 3: Evaluation of powder blend

Evaluation of core materials			
Pre compression parameter			
	Formulations		
Test	**A**	**B**	**C**
Bulk density*	0.240±0.020	0.291±0.002	0.313±0.010
Tapped density* (gm/ml)			
Hausner's ratio*	1.22±0.08	1.25±0.04	1.20±0.11
Carr's index* (%)	18.25±3.82	20.25±3.79	17±5.17
Angle of repose*(θ)	24.32±1.96	26.24±1.09	23.94±2.14

*** Values are mean ± SD, (n=3)**

Tab 4: Evaluation parameters for core tablets

Post compression parameter			
Test	**Formulations**		
	A	**B**	**C**
Diameter*(mm)	9.52±0.05	9.52±0.05	9.52±0.04
Thickness*(mm)	4.21±0.05	4.22±0.05	4.21±0.05
Weight variation*(mg)	PASS	PASS	PASS
Content uniformity* (mg)	98.19±3.76	99.51±2.31	99.11±0.94

Hardness* (kg/cm^2)	5.24±0.12	5.36±0.67	5.05±0.29
% Friability*	0.38±0.023	0.42±0.127	0.50±0.097

*** Values are mean ± SD, (n=3)**

***In vitro* release of core tablets**

The results of *in vitro* release of theophylline from different formulation (A to C) are shown in Figure 2.

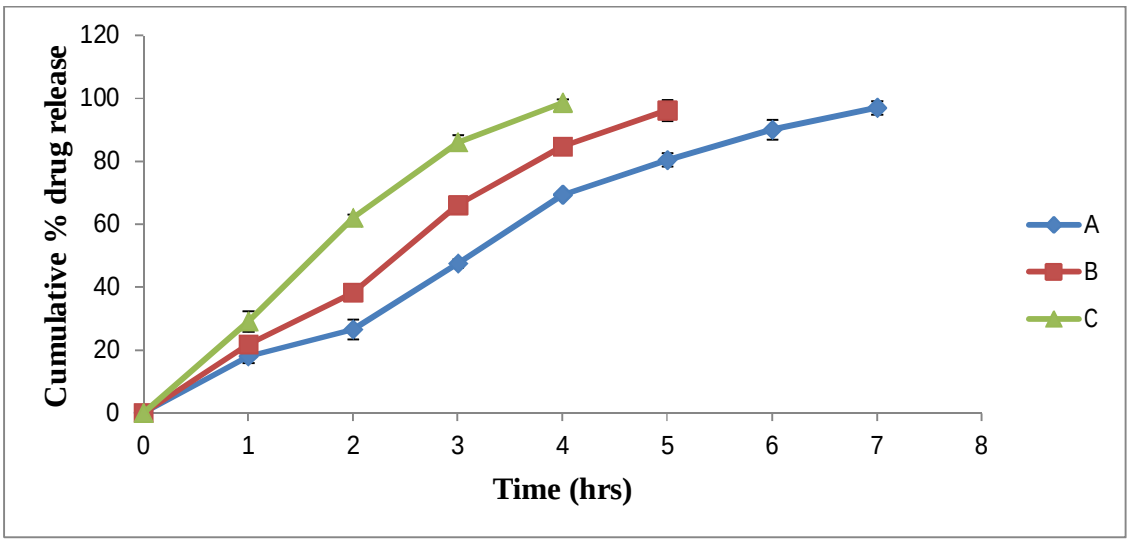

Fig 2: *In vitro* release of Theophylline from A to C formulations

It can be seen from the Figure 2 cumulative % drug release from formulations A, B and C was found to be 96.98 % (7 hrs), 96.10 % (5 hrs) and 98.57 % (4 hrs) respectively. The osmotic agent concentration increases then the osmotic pressure created inside the tablet also increases, the core compartment imbibes aqueous fluids from the surrounding environment across the membrane and dissolves the drug so the release of the drug also will increase. On the basis of satisfactory evaluation parameter with *in vitro* drug release, formulation A was selected as core material.

EVALUATION OF FILM PROPERTIES OF COATING SOLUTION

Prepare cellulose acetate coating solution with respect the concentration of 2%w/v, 3%w/v and 4% w/v of cellulose acetate in acetone. prepared solutions, in that 2% and 3% w/v 4% w/v cellulose acetate soluttion contain not clear solutions, but 4% w/v cellulose acetate soluttion contains clear and transperant film, so finally 4% w/v cellulose acetate soluttion has been taken for film coating solution utilized in differant formulations. Here P1, P2 and P3 batches contain

4% w/v cellulose acetate coating soluttions, and the evaluation of these batchs are bellow. The results of coating film of formulations P1 to P3 are shown in Table 5.

Tab 5: Evaluation of cellulose acetate coating film

Formulation Code	Folding Endurance	Tensile Strength	Elasticity
P_1	45	Good	Good
P_2	49	Good	Good
P_3	51	Good	Good

The results revealed that the formulation P_1 and P_2 have desired tensile strength, elasticity and appearance of the film. So, formulation P_1 and P_2 were selected for coating of core tablets.

EVALUATION OF FACTORIAL DESIGN FORMULATIONS

Evaluation of powder blend

The results of powder blend of formulations F**1** to F**8** are shown in Table 6.

Tab 6: Powder blend of formulations F1 to F8

Formulation	Bulk density* (gm/ml)	Tapped density* (gm/ml)	Hausner's ratio*	Carr's index*	Angle of repose*
F1	0.297±0.038	0.320±0.028	1.11±0.020	9.28± 2.16	25.82±0.34
F2	0.313±0.017	0.368±0.005	1.19±0.054	13.26±1.78	23.95±0.25
F3	0.282±0.010	0.320±0.015	1.15±0.040	12.79±2.37	23.56±0.50
F4	0.296±0.022	0.338±0.098	1.17±0.005	12.12±1.16	24.89±0.73
F5	0.300±0.014	0.357±1.018	1.17±0.020	14.21±3.42	26.17±0.76
F6	0.304±0.021	0.354±0.014	1.16±0.03	10.23±2.14	25.32±0.071
F7	0.291±0.035	0.332±0.031	1.18±0.014	11.20±1.36	24.15±0.41
F8	0.311±0.026	0.362±0.021	1.15±0.05	14.23±1.32	26.14±0.51

*** Values are mean ± SD, (n=3)**

The results of angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio indicates that powder blend has good flow property with good compressibility and suitable for direct compression method. Tablets prepared by wet granulation technique

showed uniform thickness, diameter and acceptable weight variations limit as per pharmacopoeial specifications. Hardness was found in the range of 5.5 to 6.0 kg/cm2 for all the formulations of the core tablet and the friability for all formulations was found to be less than 1% indicating sufficient mechanical integrity and strength of the prepared tablets.

Tab 7: Post compression parameters of factorial design formulation

Formulation	Diameter* (mm)	Thickness* (mm)	Hardness* (kg/cm2)	% Friability*	Weight uniformity*
F1	9.62±0.02	4.31±0.05	5.8±0.21	0.61±0.06	PASS
F2	9.65±0.03	4.34±0.06	6±0.27	0.55±0.02	PASS
F3	9.61±0.05	4.31±0.02	5.7±0.31	0.64±0.03	PASS
F4	9.64±0.06	4.33±0.01	5.9±0.32	0.59±0.04	PASS
F5	9.62±0.01	4.31±0.05	5.8±0.21	0.61±0.03	PASS
F6	9.64±0.04	4.34±0.04	6±0.24	0.55±0.04	PASS
F7	9.61±0.03	4.31±0.06	5.8±0.36	0.61±0.03	PASS
F8	9.65±0.03	4.34±0.02	6.1±0.27	0.51±0.02	PASS

*** Values are mean ± SD, (n=3)**

***In vitro* drug release study of factorial design formulations**

The results of *in vitro* release of Theophylline from different factorial formulation F1 to F8 are shown in Figure 3 and 4.

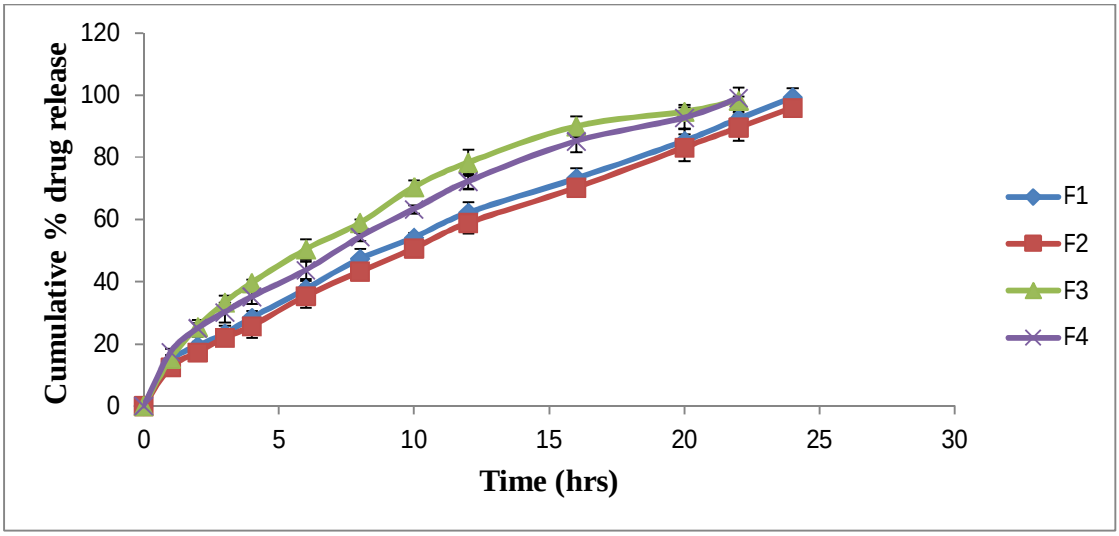

Fig 3: Drug release profile of F1 to F4

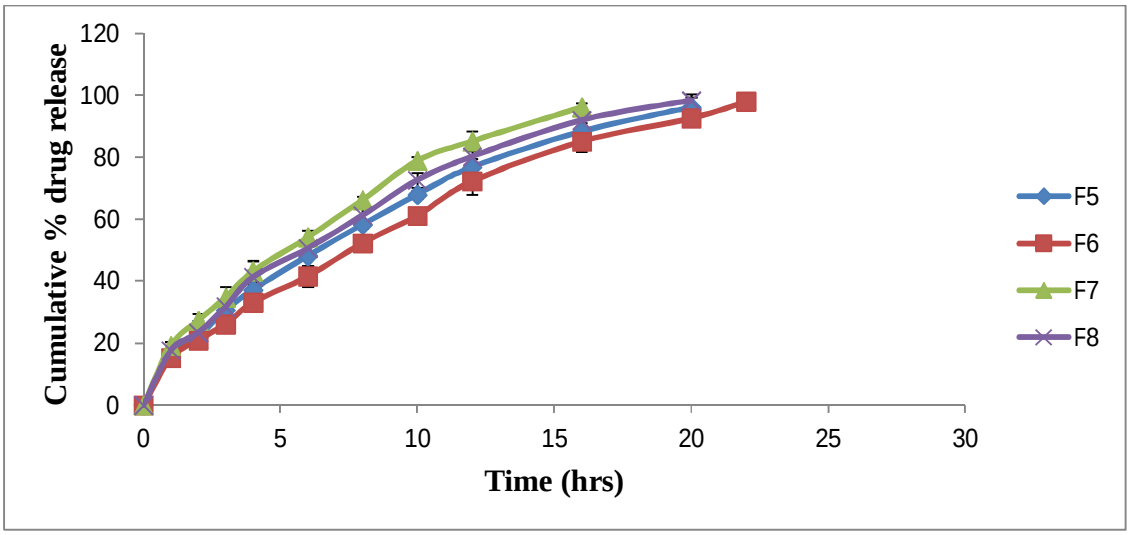

Fig 4: Drug release profile of F5 to F8

It can be evident from Figure 3 and 4 that the cumulative percentage drug release from the formulation prepared by using 2^3 full factorial design were found to be F_1 (99.32 % in 24 h), F_2 (95.91 % in 24 h), F_3 (98.28 % in 22 h), F_4 (99.05 in 22 h), F_5 (96.14 in 20 h), F_6 (98.05 in 22 h), F_7 (96.25 in 16 h) and F_8 (98.36 in 20 h).

Tab 8: Drug release kinetic data of formulation F1 to F8

Formulation	Regression Coefficient (R)			
	Zero Order	First Order	Higuchi	Krosmayer Peppas
F_1	0.989	0.914	0.957	0.941
F_2	0.985	0.900	0.941	0.947
F_3	0.939	0.840	0.930	0.924
F_4	0.985	0.883	0.963	0.912
F_5	0.964	0.857	0.964	0.946
F_6	0.971	0.885	0.959	0.915
F_7	0.976	0.818	0.952	0.909
F_8	0.952	0.892	0.966	0.927

EVALUATION OF OPTIMIZED FORMULATION F_1

To study effect of pH on drug release of optimized formulation F_1

The results of *in vitro* release of Theophylline from optimized formulation F_1 are shown in Figure 5.

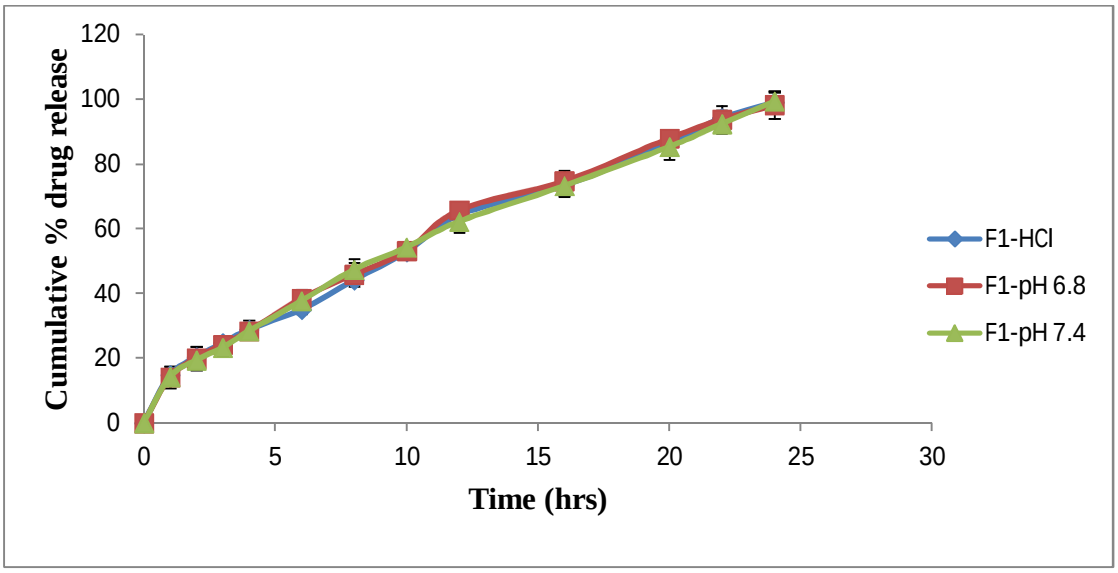

Fig 5: *In vitro* release of Theophylline from F_1 formulation in 0.1 N HCl, phosphate buffer pH 6.8 and phosphate buffer pH 7.4

It suggest that the dissolution data and dissolution profile of optimize formulation F_1 in pH 1.2 hydrochloric acid, pH 6.8 phosphate buffer and pH 7.4 phosphate buffer solutions respectively. The drug release rate in different dissolution media was almost similar. The pH of dissolution media has not significant impact on the drug release. So, the drug release from osmotic pump tablet was independent from pH.

To study effect of agitation intensity on drug release of optimized formulation F_1

The results of *in vitro* release of Theophylline from optimized formulation F_1 are shown in Figure 6.

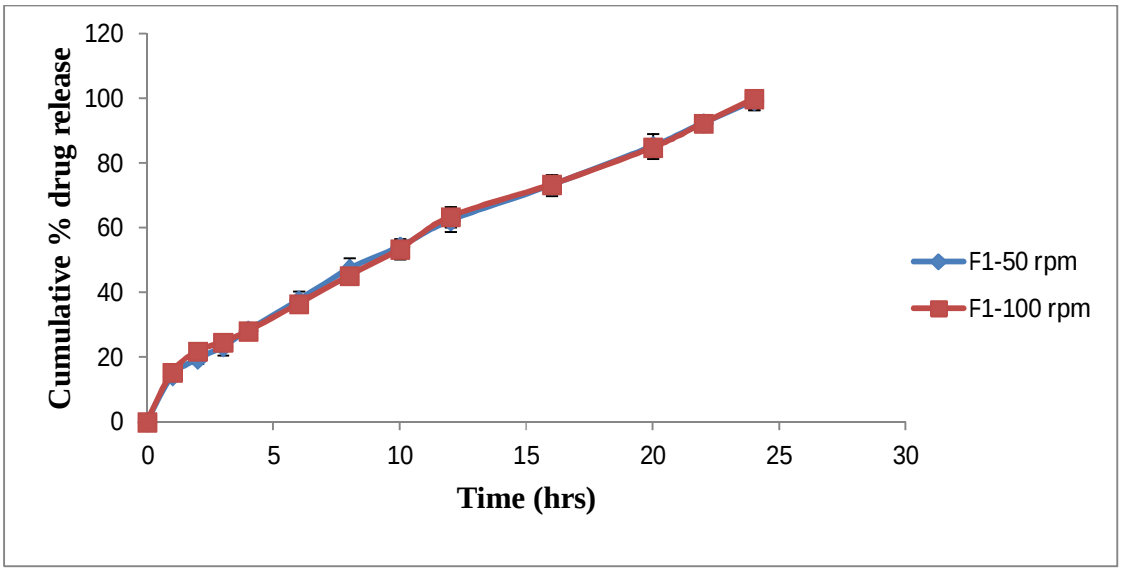

Fig 6: *In vitro* release of Theophylline from F_1 formulation at 50 and 100 rpm

It clearly evident that the dissolution data and dissolution profile of optimize formulation at 50 and 100 rpm. The drug release rate at different agitation speed was almost similar. The agitation speed of paddle has not significant impact on the drug release. So, the drug release from osmotic pump tablet was independent on agitation intensity. It could be expected that the release from the developed formulation will be independent of the hydrodynamic condition of the body.

Stability Study of Optimized Formulation F1

Short term stability studies were performed at temp of 40± 2°C/75± 5% RH over a period of one month (30 days) on the promising osmotic tablets of Theophylline (formulation F1). Sufficient number of tablets (15) were packed in amber colored rubber stopper vials & kept in stability chamber maintained at 40 ±2°C/75± 5% RH. Samples were taken at one month interval. At the end of one month period, dissolution test was performed to determine the drug release profile.

Tab 9: The results of appearance and drug content

Days	Appearance	Drug content*
0	Good	97.72±0.34
15	Stable	97.65±0.61
30	Stable	97.17±0.67

*** Values are mean ± SD, (n=3)**

Results of *In vitro* release of Theophylline from F1 formulation are given in Figure 7.

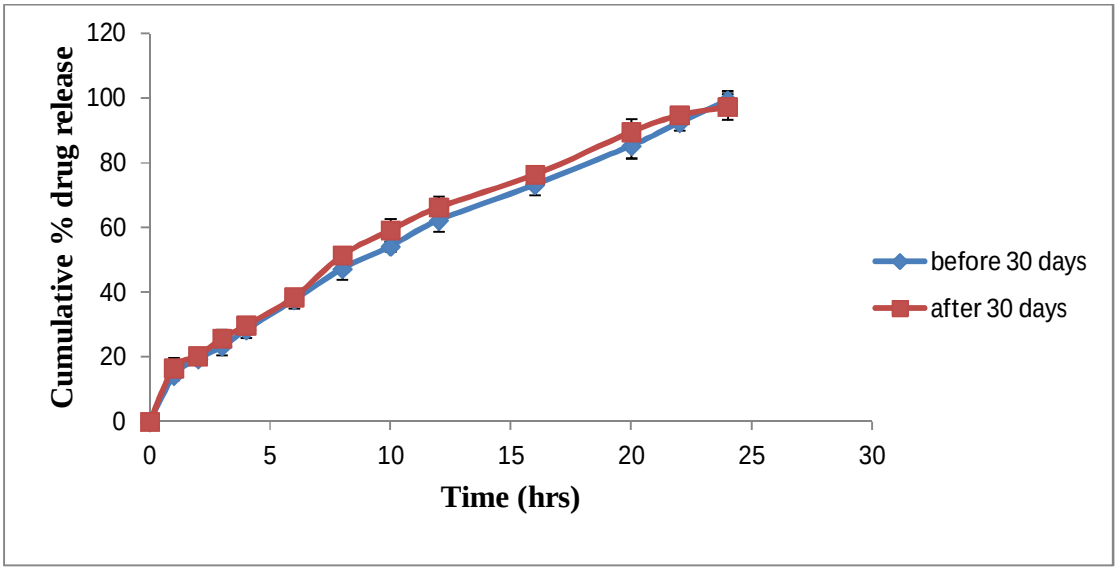

Fig 7: *In vitro* release of Theophylline from F_1 formulation before and after (30th day) stability study (40 ± 2°C and 75% ± 5% RH)

Dissolution profiles before and after storage are nearly same. The change in the drug release pattern i.e. dissolution profile was not significantly different from the one month previous tablet dissolution profile. The developed dosage form passes stability study carried out for 30 days at 40± 2°C/75± 5% RH.

CONCLUSION

Theophylline was successfully formulated as controlled porosity osmotic pump tablets to release drug at zero order release up to 24 hrs. The rate of drug release from the formulation increased with increased in concentration of osmogent, increased with increased in pore forming agent and increase with decrease in % weigh gain.

In present investigation, factorial batches F1 to F8 were prepared using 150 mg and 200 mg NaCl, 10 to 20 % w/w PEG-400 and 8 to 10 % w/w weight gain of cellulose acetate.

Among the F1-F8 batches, F1 batch containing 150 mg NaCl, 10 % w/w PEG-400 and 10 % w/w weight gain of cellulose acetate gives 14.24% drug release after 1 hr and 90 % drug release after 20.65 hrs which is nearer to theoretical release profile and mimicking the fluctuating symptoms of respiratory disease, in inflammation as an immunomodulatory effect.

Finally, it can be concluded that preparation of osmotic pump tablet can be simplified by coating the core tablet with the a pore forming agent which is likely to be most cost-effective than laser drilling.

REFERENCE

1. Stuti G, Ravindra PS and Rohitashva S, "Osmotic pumps: A review." International journal of comprehensive pharmacy. 2011, 2, 1-8.

2. Piyush G, Pankaj R and Dabeer A, "A review on osmotically regulated devices." International journal of pharmacy & life sciences. 2010, 1, 302-312.

3. Brahma PG, Navneet T and Nishi PJ, "Osmotically Controlled Drug Delivery System with Associated Drugs." Journal of Pharmacy & Pharmaceutical Sciences. 2010, 13, 571-588.

4. Thakor RS, Majmudar FD and Patel JK, "Review: Osmotic drug delivery system current scenario." Journal of pharmacy research, 2010, 3, 771-775.

5. Aditya K and Sanjay G, "An update on osmotic drug delivery patents." Pharmaceutical technology, 2003, 27, 32-39.

6. Theeuwes F, "Elementary Osmotic Pump." J Pharm Sci. 1975, 64, 1987-1991.

7. Roger RA, "Applicability of (SBE) 7m- β-CD in controlled-porosity Osmotic pump tablets." Int. J. Pharm. 2004, 286, 81-88.

8. Shailesh S, "Osmotic controlled drug delivery." Pharmainfo.net. 2008, 6.

9. Gohel MC, Parikh RK and Shah NY, "Osmotic Drug Delivery: An Update." Pharma info.net. 2009, 7.

10. Suresh VP, Prabakaran D, Paramjit S, Parijat K, Jaganathan KS and Amith R, "Modified push-pull osmotic system for simultaneous delivery of Theophylline and Salbutamol: development and in vitro characterization." Int. J. Pharm. 2004, 284, 95- 108

11. Padma VD, Patil GP, and Dabholkar RD, "Osmotic DDS: An Overview." Express Pharma Pulse, special feature. 2003, 29, 36-38.

12. Liu L, Khang G, Rhee JM and Lee HB, "Monolithic osmotic tablet system for nifedipine delivery." J. Contr. Release. 2000, 67, 309-322.

13. Tanmoy G, Amitava G, "Drug delivery through osmotic systems – An overview." Journal of Applied Pharmaceutical Science. 2011, 1, 38-49.

14. Liu L, Khang G, Rhee JM and Lee HB, "Monolithic osmotic tablet system for nifedipine delivery." Journal of control release, 2000, 67, 309-322.

15. Drug Bank- **sep-13**, http://www.drugbank.ca/search?query=theophylline+anhydrous.

16. Drugs.com- **sep-13**, http://www.drugs.com/cdi/theophylline.html.

17. Wikipedia- **sep-13**, http://en.wikipedia.org/wiki/Theophylline.

18. Drugs.com-**oct-13**, http://www.drugs.com/food-interactions/theophylline.html.

19. Rane M, Siahboomi A,"The Experimental Methods Study of Dose-Weight Proportionality in Osmotic Push-Pull Technology using Theophylline as a Model Drug",*American accociation of pharmaceutical science*, **2013**, 59, 86-120.

20. Hua Deng, Scott Vass, Piyush Patel,"Effect of Polyethylene Oxide Molecular Weight and Osmogen Content on the Performance of Push-Pull Osmotic Pump Tablets" *International journal of pharmaceutics*, **2012**, 18, 250-278.

21. http://www.ncbi.nlm.nih.gov/pubmed/6429620.

22. http://www.nhs.uk/Conditions/Asthma/Pages/MedicineOverview.aspx?condition=Asthma&medicine=Theophylline.

23. http://www.chemicalbook.com/ChemicalProductProperty_US_CB4285388.

24. Florey K. Analytical profiles of drug substances: Academic press; 1979:4:698-715.

25. Medline India, http://www.medlineindia.com/respiratory/theophylline.html, 2013.

26. USP 29-NF 26. Asian edition, Rockville, MD: United States Pharmacopeial Convention Inc. 2006; 1222-1223.

27. Gennaro AR and Remington. The Science and Practice of Pharmacy, 19th edition, Mack Publishing Co., Eastern Pennsylvania, USA, 1995;1660,1676.

28. Lachman L. The Theory and Practice of Industrial Pharmacy, 3rd edition, 1987; 336, 413.

29. Costa P and Sousa JM. "Modeling and comparison of dissolution profiles." European Journal of Pharmaceutical Sciences. 2001; 13:123-133.