OPEN ACCESS

Saudi Journal of Medical and Pharmaceutical Sciences
Abbreviated Key Title: Saudi J Med Pharm Sci
ISSN 2413-4929 (Print) | ISSN 2413-4910 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: https://saudijournals.com

Original Research Article **Pharmaceutics**

Formulation and Evaluation of Extended-Release Tablets of Oxybutynin HCL by Push-Pull Technology

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DOI: 10.36348/sjmps.2022.v08i10.002 | **Received:** 01.09.2022 | **Accepted:** 08.10.2022 | **Published:** 12.10.2022

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Abstract

The objective of this study was to formulate and evaluate Extended-release oxybutynin chloride tablets using a push-pull osmotic pump system. Oxybutynin HCL is a muscarinic antagonist used for the treatment of overactive bladder with symptoms of urinary incontinence, urgency, and frequency. PPOP are used to deliver drugs that are highly soluble in water. The drug is located in the upper compartment along with osmogent while the lower compartment consists of polymeric osmotic agents. The push pull technique has been formulated in the form of double-layer tablets by wet granulation. The nine formulations were prepared using oxybutynin chloride, HPMC, polyethylene oxide, Nacl, and other excipients, lubricants, and colouring agents. The tablets are coated with a semi-permeable membrane (cellulose acetate), followed by a film coating. The pre-compression parameters (Bulk density, tapped density, Carr's index, Hausner ratio, and angle of repose) and post-compression parameters of the extended-release tablets (Hardness, friability, weight variation, thickness, and drug content) were all within limits. An FTIR study showed no interaction between API and HPMC and all excipients at the molecular level. In vitro release studies in 0.1 N HCl, and 6.0 phosphate buffer showed that the optimized F5 formulation extended the drug release by 93% after 24 h and the release profile was similar to a product from an innovator.

Keywords: Oxybutynin HCL, Push Pull Osmotic Pump Extended Release, Bilayer, Osmogent, Film Coating.

1. INTRODUCTION

Oral controlled release systems have been preferred in all new drug delivery systems because they can deliver controlled pharmaceutical agents over a long period. Oral administration is considered the most natural, convenient, and safe due to its ease of use, patient acceptance, and cost-effectiveness. Among the existing techniques to improve the bioavailability of these drugs, the fabrication of an osmotic drug delivery system is the most appropriate one. Osmotic systems for controlled drug delivery employ an osmotic pressure gradient as the driving force to maintain plasma concentration within the therapeutic range. The drug release is independent of pH and other physiological parameters. Osmosis pumps are well known for delivering drugs with zero order rates.

A wide spectrum of osmotic devices is in existence, of which the osmotic systems are unique, dynamic, and widely employed in clinical practice. The osmotic pumps offer many advantages such as ease of manufacture, simplicity in operation, improved patient compliance with reduced dosing frequency, and a more consistent and prolonged therapeutic effect obtained with uniform blood concentration. Moreover, they are inexpensive.

A push-pull osmotic pump is a modified multi-chamber Elementary osmotic pump, which can deliver both poorly water-soluble and highly water-soluble drugs at a constant rate. They have been successfully manufactured and marketed to deliver drugs for various indications, such as hyperglycemia, hypertension, angina, for once-a-day toms of urgency, frequency, and in continuance, and asthma.

POPP looks like a typical bilayer with a semi-permeable membrane. The drug along with the osmogent is present in the upper compartment while the lower compartment consists of the polymeric osmotic substances. The drug compartment is connected to the outside environment through a delivery orifice. After

coming in contact with the aqueous medium, the polymeric osmotic layer swells and pushes the drug layer, thereby delivering the drug in a finely dispersed form through the orifice.

Oxybutynin HCL is an anticholinergic medicine used to relieve urinary and bladder problems, including frequent urination and inability to control urination, by reducing bladder muscle spasms. It competitively antagonizes the M1, M2, and M3 subtypes of the muscarinic receptor. Oxybutynin HCL is an antispasmodic and anticholinergic agent. The mechanism of action of oxybutynin chloride is that it has a direct antispasmodic effect on smooth muscle and inhibits the action of acetylcholine at the post-ganglionic cholinergic sites, thus increasing bladder capacity and delaying the initial desire to void by reducing the number of motor impulses reaching the depressor muscle. It does not block the effects of acetylcholine at skeletal muscle junctions or autonomic ganglia; nor does it affect the smooth muscle of the blood vessels. This research aims to develop Extended-release tablets of Oxybutynin HCl.

2. MATERIALS AND METHODS:

2.1. MATERIALS:

Oxybutynin HCl was obtained from Harman Finochem ltd, polyethylene oxide from Colorcon, Nacl from SD Fine-Chem Ltd, HPMC E5 was purchased from lottifine, Magnesium stearate was obtained from Peter Green, Microcrystalline cellulose was obtained as a gift sample from DFE Pharma, Butylated hydroxyl toluene (BHT) was purchased from Ratnagiri Chemicals Pvt. Ltd, cellulose acetate from Alpha chemics, iron oxide red and black iron oxide was obtained from Venator, Opadry yellow from colorcon.

2.2. INSTRUMENTS:

Tablet Compression machine (Karnawati Mumbai), UV-Visible spectrophotometer (UV 1800, Shimadzu), HPLC(Shimadzu), Auto Coater (Mark Maker Pharma), dissolution test apparatus type II-paddle (Electrolab), tablet hardness tester (Monsanto tester), electronic balance (Mettler Toledo), Roche friabilator (Electrolab),

2.3. ANALYTICAL METHOD:

2.3.1. Determination of absorption maxima:

100mg of Oxybutynin HCL drug was dissolved in 10ml water and made up to 100 ml with 0.1N HCl (stock solution). 10ml was taken from the above solution and made up to 100 ml with 0.1N HCl (100µg/ml). From this 10ml was taken and made up with 100ml of 0.1N HCl(10µg/ml) and 6.8 phosphate buffer. The samples were analysed by UV-Visible spectrophotometer (Shimadzu) and Solutions were scanned in the range of 200-400 nm.

2.3.2. Preparation of Standard Curve:

2.3.1.2. Standard plot of oxybutynin HCL using 0.1 N HCl:

100mg of pure drug Oxybutynin HCl was dissolved in 10ml water and made up to 100ml with 0.1N HCl (stock solution) in a standard flask. 10mL from the above solution was taken and adjusted to 100mL using 0.1N HCl (100µg/mL). From this 10ml was taken and made up with 100ml of 0.1N HCl (10µg/ml). The above solution was then diluted with 0.1N HCl to obtain a dilution series containing 5, 10, 15, 20 and 25µg/ml of oxybutynin per ml of solution. The absorbance of the above dilutions was measured at 210 nm using a UV spectrophotometer with a blank of 0.1N HCl. A graph was then drawn by giving a straight line with a concentration on the x-axis and absorbance on the y-axis. The Linearity of the standard curve was assessed from the correlation coefficient (R2) which was determined by least-square linear regression analysis.

2.3.2.2. Standard plot of Oxybutynin HCL using P^H 6.0 Phosphate buffer

100mg of pure drug Oxybutynin HCl was dissolved in 10ml water and made up to 100ml with P^H 6.0 phosphate buffer (stock solution) in a standard flask. 10mL from the above solution was taken and adjusted to 100mL using P^H 6.0 "phosphate buffer" (100µg/mL). From this 10ml was taken and made up with 100ml of P^H 6.0 phosphate buffer (10µg/ml). The above solution was then diluted with 0.1N HCl to obtain a dilution series containing 5, 10, 15, 20 and 25µg/ml of oxybutynin per ml of solution. The absorbance of the above dilutions was measured at 210 nm using a UV spectrophotometer with a blank of P^H 6.0 phosphate buffer. A graph was then drawn by giving a straight line with a concentration on the x-axis and absorbance on the y-axis. The Linearity of the standard curve was assessed from the correlation coefficient (R2) which was determined by least-square linear regression analysis.

2.4. FTIR studies:

The compatibility studies of the oxybutynin HCl, associated polymers and excipients were analyzed using an FTIR spectrophotometer by the KBr pellet method. An accurately weighed amount of Sample was mixed with KBr and forced into a disc with a manual press. The spectrum was scanned in the wavelength region of 4000-400cm^{-1}. The characteristic absorption peaks of oxybutynin hydrochloride were obtained at different wave numbers in different samples. The peaks obtained in the spectra of each formulation correlate with the drug spectrum peaks.

3. PREPARATION OF EXTENDED-RELEASE OXYBUTYNIN HCL TABLETS:

3.1. DRUG LAYER (PULL LAYER):

Oxybutynin HCl, polyox N10, NaCl, and MCC were accurately weighed and sieved through a

#40 mesh and collected the mixture in a polybag. Transfer the sifted mixture to a clean and dry Rapid Mix Granulator and mix for 10mins at a slow impeller. Slowly add the dispensed amount of BHT and HPMC E5 to the IPA and stir continuously until a clear solution is formed under mechanical stirring. Add the granulation solution slowly to the dry mix and blend in RMG with impeller speed off. The wet mixture was kneaded for 30 to 60 seconds with an impeller speed of 100 rpm and a chopper speed of 1000 rpm. Set impeller speed to 20 rpm and turn off the chopper, unload granules. The wet mass was transferred to a rapid drier and dried for 45mins. Drying was confirmed by subjecting it to LOD at 70℃ temperature in auto mode. The dried granules have been sieved through #20 mesh. Oversized pellets are milled through a 1mm screen fitted to multi mill, milled until all the pellets pass through #20 mesh. Weighed quantity of magnesium stearate and red iron oxide was passed through #60 mesh and added to above granules and lubricated for 5 mins in blender at 10rpm.

3.2. PUSH LAYER:

Polyox 303, MCC, and NaCl were accurately weighed and sieved through a #40 mesh and collected the mixture in a polybag. Transfer the sifted mixture to a clean and dry Rapid Mix Granulator and mix for 10mins at a slow impeller. Slowly add the dispensed amount of BHT and HPMC E5 to the IPA and stir continuously until a clear solution is formed under mechanical stirring. Add the granulation solution slowly to the dry mix and blend in RMG with impeller speed off. The wet mixture was kneaded for 30 to 60 seconds with an impeller speed of 100 rpm and a chopper speed of 1000 rpm. Set impeller speed to 20 rpm and turn off the chopper, unload granules.

OXYBUTYNIN HCI ER TABLETS 10 mg							
INGREDIENTS	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**
PULL LAYER (DRUG LAYER)							
Dry Mix							
Oxybutynin HCL	10.0	10.0	10.0	10.0	10.0	10.0	10.0
NaCl	16.30	12.00	10.00	8.50	6.88	7.10	6.46
Polyox N10	61.50	65.82	67.82	69.32	70.94	79.24	79.24
BHT	0.07	0.07	0.07	0.07	0.07	0.07	0.07
HPMC E5	1.85	1.85	1.85	1.85	1.85	1.85	1.85
IPA	qs	qs	qs	qs	qs	qs	qs
Magnesium Stearate	0.23	0.23	0.23	0.23	0.23	0.23	0.23
Ferric oxide red	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Pull layer weight (mg)	90.00	90.00	90.00	90.0	90.00	90.00	90.00
PUSH LAYER							
Dry Mix							
NaCl	21.50	19.00	18.60	18.60	18.60	18.60	18.60
Polyox 303	34.67	37.17	37.57	37.57	37.57	37.57	37.57
MCC	0.03	0.03	0.03	0.03	0.03	0.03	0.03
BHT	0.05	0.05	0.05	0.05	0.05	0.05	0.05
HPMC E5	3.00	3.00	3.00	3.00	3.00	3.00	3.00
IPA	qs	qs	qs	qs	qs	qs	qs
Magnesium Stearate	0.15	0.15	0.15	0.15	0.15	0.15	0.15
Black iron oxide	0.60	0.60	0.60	0.60	0.60	0.60	0.60
Push layer Weight (mg)	60.00	60.00	60.00	60.00	60.00	60.00	60.00
Total tablet weight (mg)	150.00	150.00	150.00	150.00	150.00	150.00	150.00
Semipermeable Membrane							
Cellulose Acetate	27	27	27	27	27	27	27
PEG 6000	3	3	3	3	3	3	3
Acetone	552.9	552.9	552.9	552.9	552.9	552.9	552.9
Purified water	17.1	17.1	17.1	17.1	17.1	17.1	17.1
Total tablet weight (mg)	180.00	180.00	180.00	180.00	180.00	180.00	180.00
FILM COATING							
Opadry Yellow	5	5	5	5	5	5	5
Purified water	45	45	45	45	45	45	45
Total tablet weight (mg)	185.00	185.00	185.00	185.00	185.00	185.00	185.00

3.3. COMPRESSION AND COATING:

Bilayer tablets were compressed using two different blends, that is, pull layer and push later using 7.6 mm diameter round punches. The tablets were coated with cellulose acetate solution prepared in water and acetone as a solvent system until desired weight

gain is achieved to form a semi-permeable coating. CA-coated tablets were drilled to form the desired orifice using a laser drilling machine. Drilled tablets were further coated with Opadry film coating dispersion till desired weight gain was achieved.

4. EVALUATION OF OXYBUTYNIN HCL EXTENDED-RELEASE TABLETS:

4.1. EVALUATION OF PRE-COMPRESSION PARAMETERS:

4.1.1. Angle of Repose:

The frictional force of loose powder can be measured by the angle of repose (θ). It is defined as the maximum angle possible between the surface pile of powder and the horizontal plane. It was measured by using the fixed funnel method. The powder mixture was poured from a funnel that can be raised vertically until a maximum cone height (h) was obtained. The radius of the pile of powder was measured. The angle of repose was calculated by using the following formula given below:

$\theta = \tan^{-1}(h/r)$

Where,
θ = Angle of repose
h = Height
r = Radius

4.1.2. Bulk Density:

The bulk density of the powder depends on particle size distribution, particle shape and the tendency of particles to adhere together. 30g of the powder blend was introduced into a dry 100mL cylinder, without compacting. The powder was carefully levelled without compacting and the unsettled apparent volume, Vo, was determined.

$\rho b = W / Vb$

Where,
ρb = Apparent Bulk Density
w = weight of the sample
Vb = bulk volume of powder

4.1.3. Tapped Density:

It was determined by placing in a graduated cylinder, the known mass of drug, excipient blend, on mechanical tapping apparatus, which was operated for a fixed time for a number of taps until the powder bed volume has reached a minimum constant. Tapped Density was calculated by using the formula given below:

$\rho t = W / Vt$

Where,
W = Weight of the powder
Vt = Tapped Volume of the powder

4.1.4. Compressibility Index or Carr's Index (CI):

Initially weighed quantity of powder was measured and thus transferred to a graduated cylinder and volume was measured. A lid was closed on the top of the graduated cylinder and tapped on the hard surface from a height until the volume of the powder blend is maintained constant, the final volume was measured. The bulk density and tapped density were calculated by using the following equation;

Carr's Index = $(\rho t - \rho b) / \rho t$ 100

Where,
ρb = Bulk Density
ρt = Tapped Density

4.1.5. Hausner's Ratio (HR):

The ratio of tapped density to bulk density indicates the flow properties through Hausner's ratio. The ideal range should be between 1.2 and 1.5. HR was calculated by the formula:

$HR = \rho t / \rho t$

Where,
ρb = Bulk Density
ρt = Tapped Density

4.2. EVALUATION OF POST-COMPRESSION PARAMETERS:

4.2.1. Weight variation test:

Twenty tablets selected from each formulation were individually weighed using a Mettler Toledo analytical balance. The average weight of the tablets and standard deviation were calculated. The test is passed when not more than two tablets deviate from the average weight.

USP Standards	Max. % Difference Allowed	BP/ IP Standards
130 mg or less	10 %	84 mg or Less
130 mg – 324 mg	7.5 %	84 mg – 250 mg
More than 325 mg	5 %	More than 250 mg

Limits for Tablet Weight variation test:

4.2.2. Hardness

Hardness indicates the ability of the tablet to withstand mechanical shock during handling. For each formulation, the tablet hardness (n=6) was determined by using a Monsanto Hardness tester. It is expressed in kg/cm^2.

4.2.3. Friability:

It was determined by the Roche friabilator. From each batch, 10 tablets are accurately weighed and

placed in the friabilator. The apparatus was operated at 25 rpm for4mins and tablets were observed during rotation. The tablets are then taken up after 100 rotations, dedusted, and reweighed. The percentage of weight loss was calculated. The percentage friability of the tablets was calculated by the given formula:

% Friability = (W1-W2) / W1 X 100

Where,

W1 = Initial Weight of tablets

W2 = Final Weight of tablets

4.2.4. Thickness:

Five tablets were randomly selected from individual formulations and the thickness was measured by Digital Vernier calipers.

4.2.5. Drug Content:

To determine the drug content, 10 tablets were taken and crushed, and the equivalent weight of powder was accurately weighed and placed in a 100ml volumetric flask to prepare 100ppm of phosphate buffer pH6.0 from this 1ml was diluted to a 10ml flask (10ppm). The sample was measured at λmax 210nm using a Shimadzu UV spectrophotometer. The actual concentration of the sample was determined from the calibration curve of Oxybutynin Hydrochloride prepared using Phosphate buffer pH 6.0.

4.2.6. In-vitro Drug Release Studies:

In vitro, drug release studies of prepared extended-release tablets were performed using a Type 2 (paddle) USP apparatus at 37 °C ± 0.5 °C, 50 rpm, and a medium volume of 900ml over 24 hours. rice. The dissolution studies were performed in 0.1N HCl for 2 hours and further in phosphate buffer 6.0 for up to 24 hours under sink conditions. At regular time intervals, 5ml samples were withdrawn from the dissolution medium and replaced with fresh medium to maintain a constant volume. The samples are then filtered through the Whatman filter paper. The oxybutynin HCl content of each sample was analyzed by UV spectroscopy at λmax of 210nm after appropriate dilution.

5. RESULTS AND DISCUSSION

The present study aimed to develop Extended-release tablets of Oxybutynin using various polymers. All the formulations were evaluated for physicochemical properties and *in vitro* drug release studies.

PREFORMULATION STUDIES:

Table-1: API characterization

Colour	White crystalline powder,
Taste	Bitter
Odour	Characteristic
Melting point	125-130℃
Solubility	Freely soluble- water, methanol Soluble- acetone, IPA
Assay	99.8%

Calibration curve of Oxybutynin Hcl:

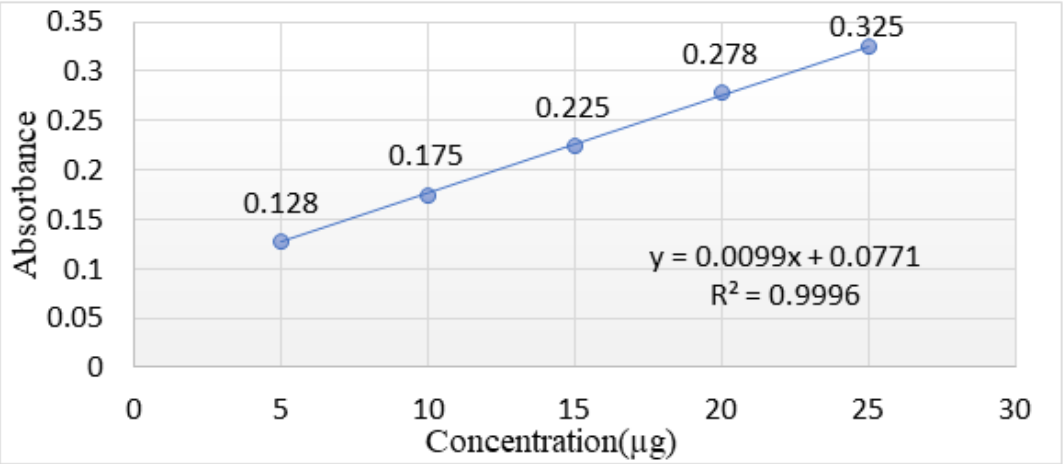

Fig-1: Calibration curve of Oxybutynin HCL in 0.1N HCL at 210nm

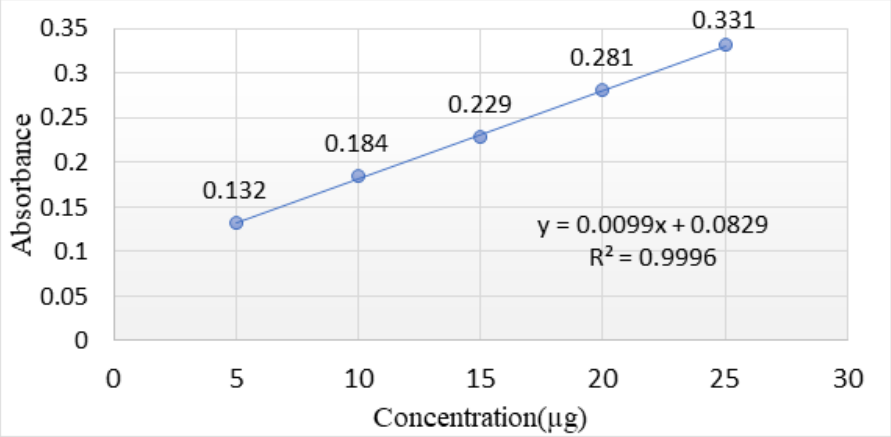

Fig-2: Calibration curve of Oxybutynin HCL in P^H 6.8 Phosphate buffer at 210nm

FTIR SPECTRUM

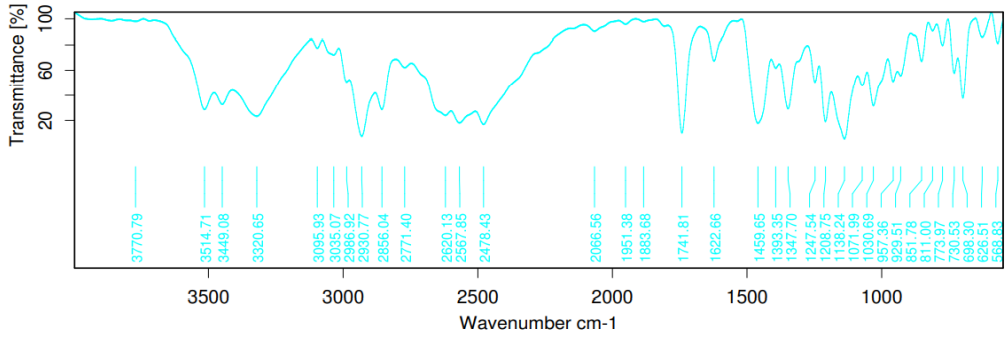

Fig-3: FTIR Spectra of Oxybutynin HCL

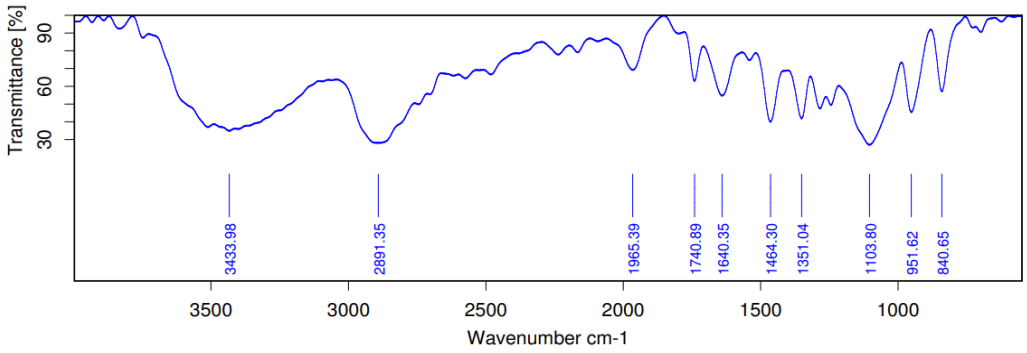

Fig-4: FTIR Spectra of Finished Product

Table-4: Evaluation parameters of the pre-compression blend of Drug Layer

Formulation	Bulk density (gm/ml)	Tapped density (gm/ml)	Angle of repose(θ)	Hausner's ratio	Carr's Index
F1	0.50 ±0.03	0.61±0.06	32.5±0.07	1.17±0.01	25±0.03
F2	0.58 ±0.02	0.61±0.07	31.5±0.06	1.12±0.01	25±0.05
F3	0.57 ±0.03	0.60±0.05	30.0±0.04	1.25±0.02	23±0.02
F4	0.49 ±0.03	0.59±0.06	30.5±0.07	1.22±0.01	24±0.03
F5	0.51 ±0.03	0.62±0.06	32.5±0.08	1.27 ±0.01	21±0.06
F6	0.53 ±0.04	0.60±0.02	34.5±0.07	1.29±0.06	22±0.03
F7	0.52 ±0.02	0.61±0.07	31.5±0.06	1.15±0.01	25±0.04

* All values were expressed as mean±standard deviation (n=3)

Table-5: Evaluation parameters of the pre-compression blend of Push Layer

Formulation	Bulk density (gm/ml)	Tapped density (gm/ml)	Angle of repose(θ)	Hausner's ratio	Carr's Index
F1	0.50 ±0.03	0.60±0.06	30.5±0.07	1.17±0.01	25±0.03
F2	0.54 ±0.02	0.61±0.04	31.5±0.06	1.12±0.06	25±0.04
F3	0.57 ±0.03	0.60±0.05	31.0±0.04	1.25±0.02	23±0.06
F4	0.50 ±0.03	0.59±0.01	30.5±0.06	1.21±0.01	24±0.03
F5	0.58 ±0.04	0.65±0.02	31.5±0.08	1.25 ±0.04	22±0.06
F6	0.56 ±0.03	0.64±0.06	30.5±0.07	1.27±0.03	21±0.02
F7	0.57 ±0.03	0.61±0.07	31.4±0.06	1.15±0.01	24±0.04

* All values were expressed as mean±standard deviation (n=3)

The bulk density of the pull and push layer blend was found to be between 0.49g/ml to 0.59g/ml. Tapped density was found to be between 0.59g/ml to 0.65g/ml. From these values, Carr's index and Hausner's ratio were calculated respectively. Carr's index for all the formulations was found to be between 21% - 25% and Hauser's ratio from 1.12-1.29 which reveals that the blends have good flow character. The angle of repose of different formulations was ≤ 34.5º which indicates that the material had good flow properties.

Table-6: Evaluation parameters of the post-compression tablet

Formulation	Weight variation (mg)	Thickness (mm)	Hardness (N)	Friability (%)	Diameter (mm)	Drug Content (%)
F1	185.2±7.51	4.4±0.12	25±1.51	0.05±0.40	7.60±0.12	98.6±0.12
F2	183.2±7.22	4.0±0.11	24±1.40	0.15±0.62	7.61±0.10	103.1±0.11
F3	186.2±6.93	4.2±0.17	26±1.01	0.52±0.30	7.65±0.13	101.5±0.03
F4	184.2±7.02	4.3±0.16	25±1.50	0.15±0.40	7.62±0.11	99.6±0.12
F5	185.0±7.50	4.1±0.11	25±1.22	0.63±0.14	7.64±0.12	99.8±0.10
F6	186.1±7.90	4.2±0.12	25±1.53	0.15±0.42	7.65±0.12	99.1±0.12
F7	184.9±7.51	4.5±0.10	25±1.60	0.11±0.10	7.65±0.16	99.8±0.11

* All values were expressed as mean±standard deviation (n=3)

Each formulation of prepared Extended released tablets of Oxybutynin HCL(F1-F7) was evaluated for various post-compression parameters like weight variation, friability, hardness, thickness, drug content and in-vitro dissolution studies. The weight variation of the tablets was in the range of 184.2 to 186.1% which lies in an acceptable range. Friability values of 0.05% to 0.15% showed that the formulations are physically stable to mechanical shocks during handling and transportation. The friability of the prepared tablets European and US pharmacopoeias states that a loss up to 1% is acceptable for friability. The hardness of all the formulations F1 to F7 ranged from 24 to 26N with good mechanical strength. Among all the formulation, F5 showed highest hardness, this could be due to presence of both Nacl and Mcc in the formulation. The thickness values of the all formulations ranged from 4.0 to 4.5mm. The drug content uniformity of the formulations was ranged between 98.6% -103.1. The hardness data demonstrated that all tablets passed the test as per USP. The drug content for all coated tablet formulations was good and lied within the specified limit.

Table-7: Invitro Drug Release Profile of Oxybutynin HCL Extended Release Tablets

Time(hrs)	F1(mg/tab)	F2(mg/tab)	F3(mg/tab)	F4(mg/tab)	F5(mg/tab)	F6(mg/tab)	F7(mg/tab)
0	0	0	0	0	**0**	0	0
2	14.5±0.39	5.5±1.01	17.5±2.04	10.4±1.84	2.2±1.04	6.8±0.34	12.3±4.02
4	25.7±2.12	14.8±0.12	29.4±4.32	19.8±0.12	9.9±0.11	15.4±4.06	19.6±1.34
6	34.9±0.03	28.4±2.09	38.3±0.19	27.6±4.99	21.1±2.31	26.9±1.25	23.9±0.68
8	49.5±1.71	37.6±0.13	46.6±1.91	49.7±0.76	31.2±1.06	37.6±2.04	31.2±1.68
10	59.7±4.57	42.8±0.67	51.7±4.5	60.2±2.07	41±2.01	43.3±0.77	40.8±0.33
12	70.2±0.77	54.3±0.92	59.8±1.12	67.9±0.92	53.5±1.22	56.9±1.64	46.4±1.88
14	78.7±1.87	66.4±1.07	65.1±1.06	72.7±1.77	64.7±1.97	69.5±1.07	52.9±2.31
16	83.5±2.16	71.8±1.06	74.6±0.06	80.6±0.12	74.6±0.7	79.3±0.36	60.1±1.64
18	88.6±0.91	76.2±0.91	81.8±0.99	84.1±2.01	82.7±2.15	86.8±1.21	68.6±4.1
20	91.3±0.74	81.3±1.74	83.9±1.04	86.5±0.34	88.3±1.66	90.4±2.14	77.4±2.14
22	94.9±2.37	86.2±4.33	88.1±0.97	90.8±2.37	91.1±0.27	93.5±0.66	82.7±0.99
24	98.1±4.05	90.3±2.05	91.4±1.05	94.9±1.05	93±0.98	96.1±0.18	89.2±1.32

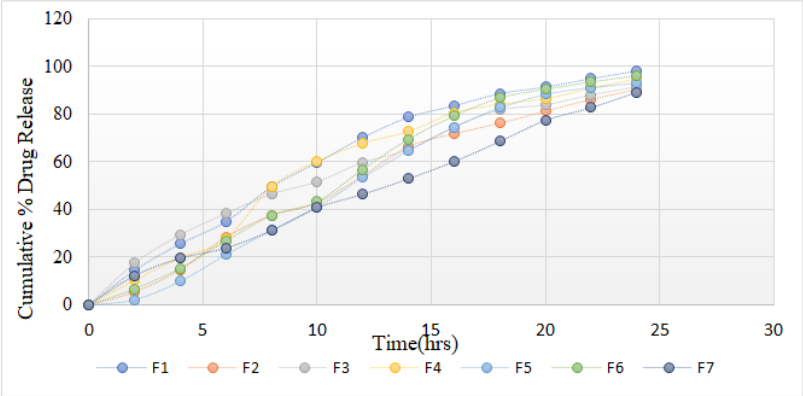

Fig-5: Invitro drug release profile of Formulations

All the formulations were subjected to in-vitro dissolution studies and results are shown in table no.4 and Fig No.5.The results reveal that release profiles of Oxybutynin HCL tablets containing varying proportions of PEO, HPMC E5 and NaCl i.e. batch F1-F7 showed drug release as given in table No. 4 in 0.1N HCL and 6.0 pH phosphate buffer, drug release is slow which may be due to osmotic pressure generated inside the tablet. The drug release occurs when solvent penetrates through the dry matrix, then dissolution and diffusion of drug through the resultant orifice causes the release of drug through the orifice. This shows that concentration of osmotic agent controls the drug release and size of the orifice. In-vitro release studies of all the formulations were also compared and evaluated. Formulation F1, F2, F3, F4, F5, F6 and F7 showed the release up to 98.1%, 90.3%, 91.4%, 94.9%, 93%, 96.1%, and 89.2% respectively at the end of 24 h. The results showed that the drug release profile of formulation F5 resembles formulation drug release as per the USP monograph.

6. CONCLUSION

The FTIR peak values of oxybutynin HCl, PEO, HPMC, BHT and all excipients are very much close to FTIR spectra of the optimized oxybutynin HCl tablet push-pull technique, indicating no existence of the interaction between the oxybutynin HCl, and all excipients. The developed formulation reduced the dosing frequency, with minimal side effects and was as effective in an osmotic controlled release oral delivery system. From the investigation studies found that the standard graph was given that regression analysis R^2 value was 0.999 in 0.1 N HCl and 0.99 in pH 6.8 phosphate buffer. The FTIR studies were shown good compatibility between the drug and excipients. All the pre and post-compression studies such as Bulk density, tapped density, angle of repose, Carr's index, Hausner's ratio, Weight variation, Thickness, Hardness, and Drug content were found to be within limits. . In vitro drug release profile of Optimised formulation was found to be 93.1 for 24hrs. A porous osmotic pump-based drug delivery system can be designed for CR of the highly water-soluble drug oxybutynin. The results show that the rate of drug release can be controlled through the osmotic pressure of the core, pore former, and membrane weight. The release from developed formulations was independent of the pH and hydrodynamic conditions of the body. Oxybutynin HCL drug release from the developed formulations was inversely proportional to the osmotic pressure, confirming that osmotic pumping is the major mechanism of the drug release.

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