Design & Characterization of Timolol Maleate Osmotic Drug Delivery System

Presented By

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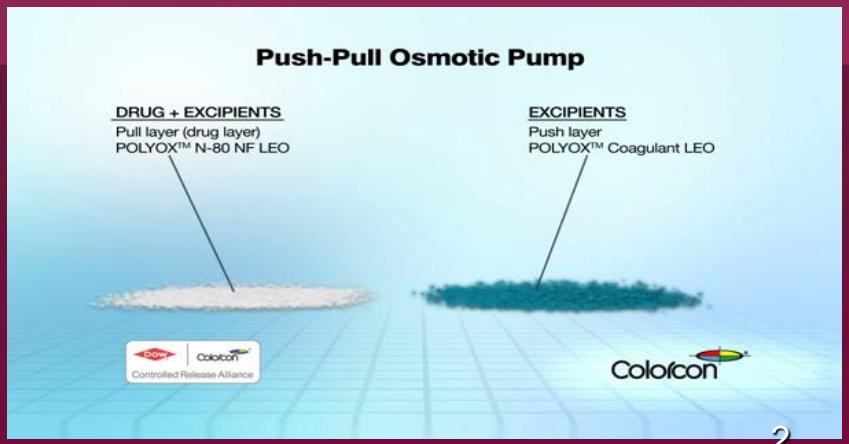
INTRODUCTION

- Osmotic drug delivery system.
- Push pull osmotic drug delivery system.

Oral Osmotic Tablet

- Single osmotic pump
  - Elemantary osmotic pump (EOP)
  - Controlled porosity osmotic pump
  - Osmotic bursting osmotic pump
- Multi-chamber osmotic pump
  - Push pull osmotic pump (PPOP)
  - Sandwich osmotic tablets (SOTS)

Push-Pull Osmotic Pump (PPOP) Tablet



❖*Push pull osmotic drug delivery system.*

Core Tablet:

Layer 1: API ± Polymer

Layer 2: Polymeric osmotic agents

Coat: Semi permeable membrane with (or) without delivery orifice.

It is a bilayer tablet coated with semi permeable membrane.

The PPOP system consists of two compartments separated usually by an elastic diaphragm. The upper compartment contains the drug and is connected to the outside environment via a small delivery orifice.

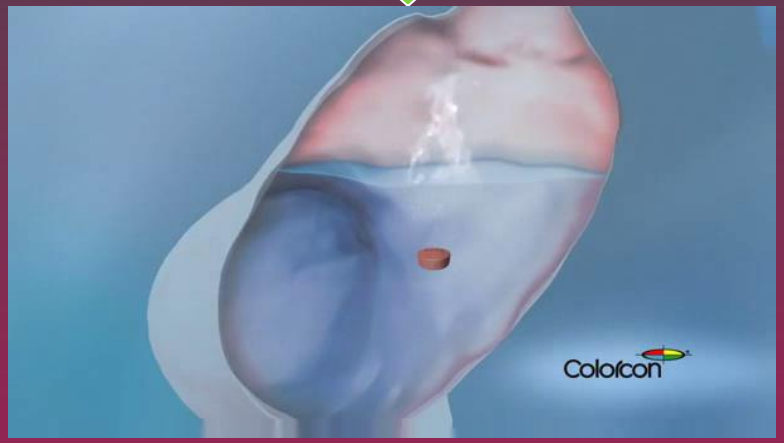
PPOPconsists of a bi-layer tablet core surrounded by a laser drilled semi-permeable membrane.

Upon contact with the aqueous fluids, the second layer swells and thereby supplying the driving force against the drug layer.

Subsequently, the

drug suspension generated in the first layer is delivered via the orifice.

Mechanism of Drug Release from PPOP Tablets



Use Design of Experiments (DOE) to

- Develop Better Products Faster.
- Improve Product/Process Performance.
- Reduce Experimental Effort and Time by 50 to 90%.
- DOE helps to pin point the sensitive parts and sensitive areas in designs that cause problems in Yield
- Designers are then able to fix these problems and produce robust and higher yield designs prior going into production.

AIM AND OBJECT OF THE STUDY

- The present work is aimed at developmenmt of extended release formulations of Timolol maleate (TM) Based on Osmotic Technology .
- In this study two-layer push pull osmotic tablet system was developed.
- This study was intended to study the influence of tablet core variable.

Materials

S.No	Category	Material	Source
1.	Active Pharmaceutical Ingredient	Timolol maleate	Ven Petro-Chem & Pharma, Mumbai.
2.	Polymer	**Polyox N-80**	Colorcon Asia Pvt. Limited Goa
3.	Polymer	**Polyox WSR Coagulant**	
4.	Coating Material	Opadry CA	
5.	Osomogen	**Sodium Chloride**	S.D Fine Chemicals, Mumbai
6.	Binder	**PVP K-30**	
7.	Lubricant	Magnesium Stearate	
8.	Glidant	Talc	
9.	Granulating Solvent	Isopropyl Alchol	
10.	Coating Solvent	Acetone	

DRUG PROFILE

- ***Name*** : Timolol Maleate

- ***Solubility*** : Freely soluble in water; soluble in ethanol and methanol. Sparingly soluble in chloroform, practically insoluble in ether and in cyclohexane.

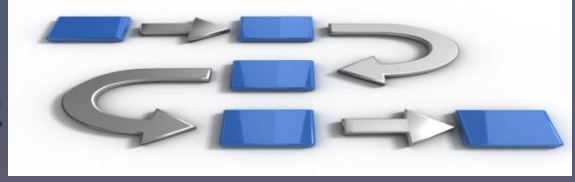
- ***Pharmacokinetics***
  - Completely absorbed (about 90%) from the GIT but it is subject to moderate first-pass metabolism.
  - Bioavailability – 60%
  - T_{max} - Peak plasma concentration occurs about 1-2 h.
  - It has low to moderate lipid solubility.
  - Protein binding is reported to be low.
  - A plasma half-life ($t_{1/2}$) is 4 h.
  - It is extensively (80%) metabolized in liver, the metabolites being excreted in urine together with some unchanged timolol.
  - It crosses the placenta & appears in breast milk.

Statistical Formulation Design

- A Response Surface Method (RSM) was used to optimize the formulations. The design consists of 4 factors at 2 levels.

Factor	Actual Values		Coded Values	
	Low	High	Low	High
Factor A (Polyox N-80)	70 %	95%	-1	+1
Factor B (Polyox WSR Coagulant)	50 %	70 %	-1	+1
Factor C (Sodium Chloride)	30 %	40 %	-1	+1
Factor D (Opadry CA)	5 %	8 %	-1	+1

Manufacturing Steps for PPOP Tablets



PULL LAYER

- Blending
- Granulation
- Drying
- Milling
- Lubrication

PUSH LAYER

- Blending
- Granulation / Direct Mixing
- Drying
- Milling
- Lubrication

- Compression of Bi-layer Tablet
- Coating of Bi-layer Tablet by Semi-preamble Coat
- Drying

Evaluation of Precompression Blend

- Bulk density (g/mL)

  BD = Weight of the powder/Volume of the packing

- Tapped density (g/mL)

  TD = Weight of the powder / Tapped volume of the packing

- Carr's Index (%)

  C.I (%) = [(TD - BD) / TD] x 100

- Angle of Repose (θ)

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

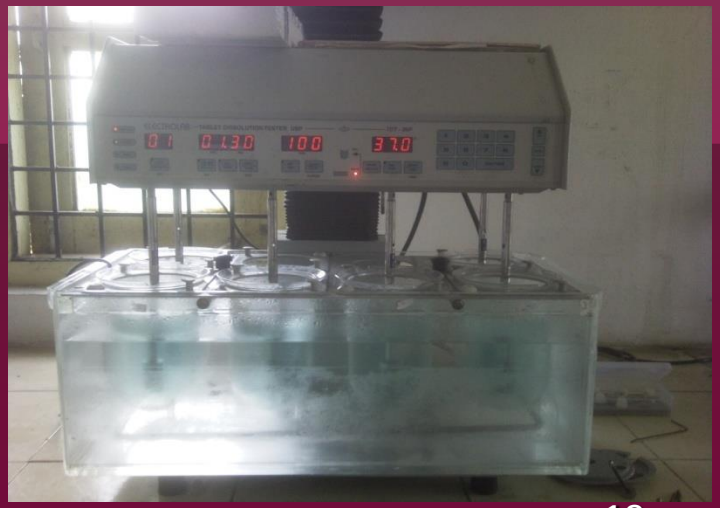
  where h and r are the height and radius of the powder cone.

- Hausner's Ratio = TD/BD *(Lachman et al., 1987).*

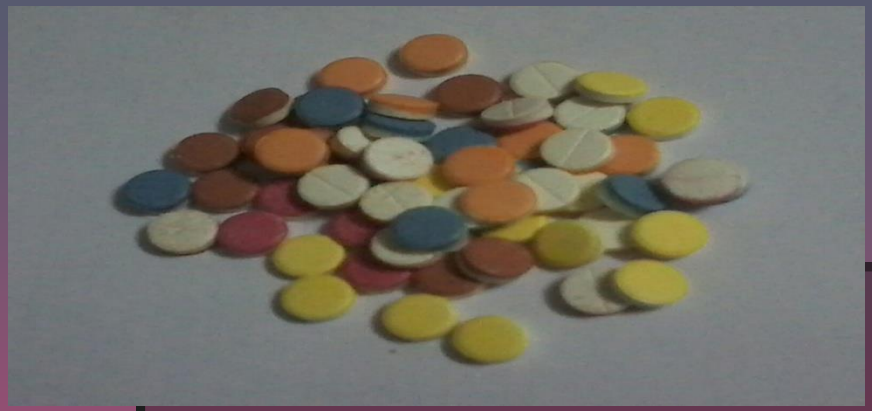
In vitro DISSOLUTION

- Apparatus : USP Dissolution Apparatus Type II (Paddle)
- Dissolution Volume : 900 ml
- Dissolution Medium:
  - 0.1 N Hydrochloric Acid — For First 2hrs
  - pH 6.8 Phosphate Buffer — For remaining 22hrs

- Aliquot Volume : 5mL
- Replishing Volume : 5 mL
- Temperature : 37±0.5°C
- RPM:
  - 100 rpm — 0.1 N Hydrochloric Acid
  - 50 rpm — pH 6.8 Phosphate Buffer.



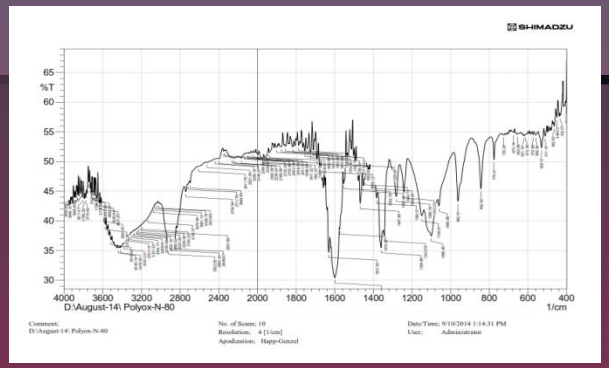
Formulations



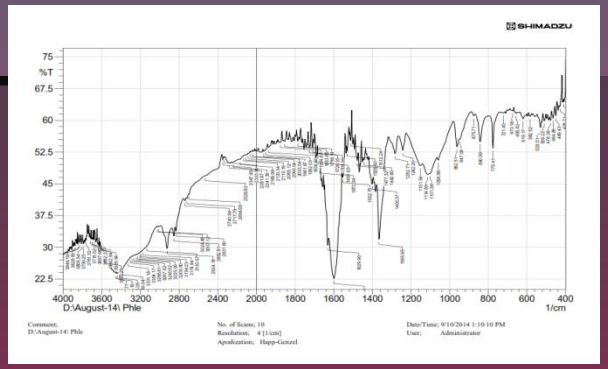
Formulations After In Vitro Dissolution

RESULT AND DISCUSSION

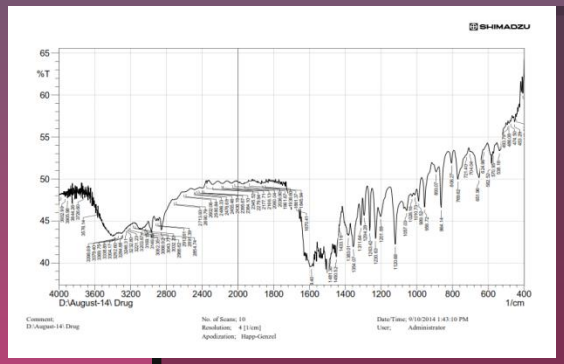
FT-IR SPECTRUM OF Polyox N 80



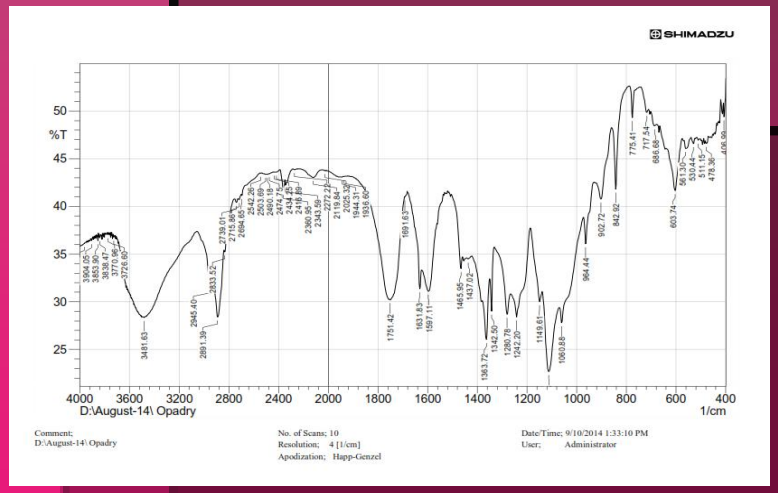
FT-IR SPECTRUM OF Polyox WSR Couglant



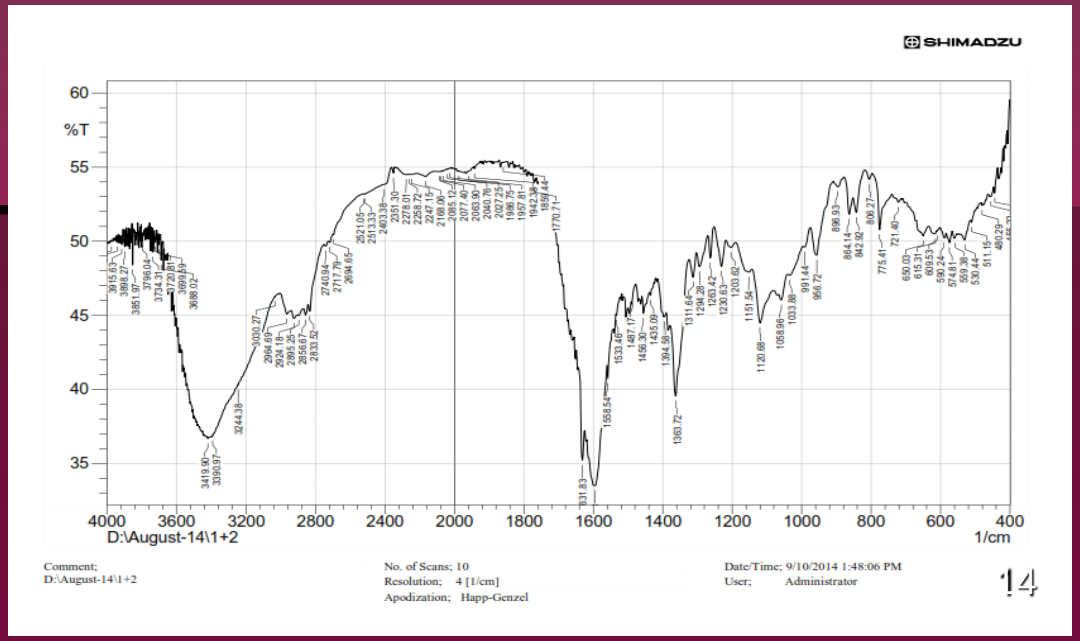
FT-IR SPECTRUM OF Timolol Maleate



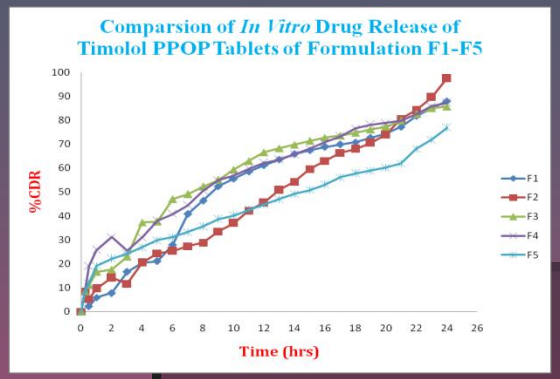
FT-IR SPECTRUM OF Opadry CA

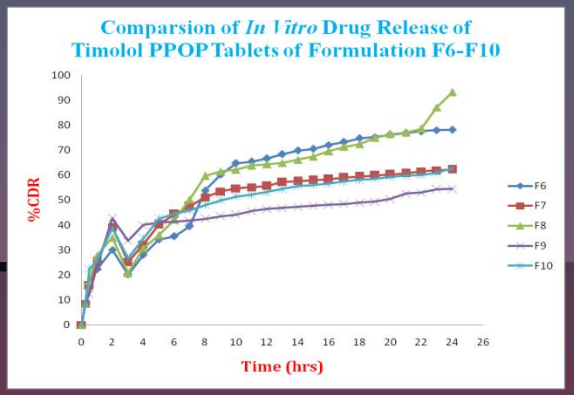


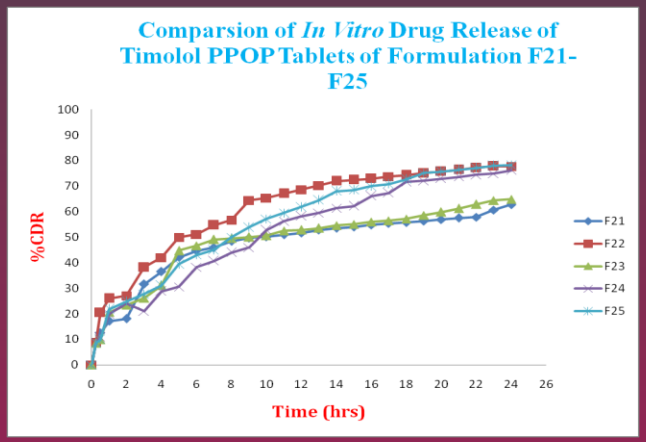
FT-IR SPECTRUM OF Optimized Formulation (F2)

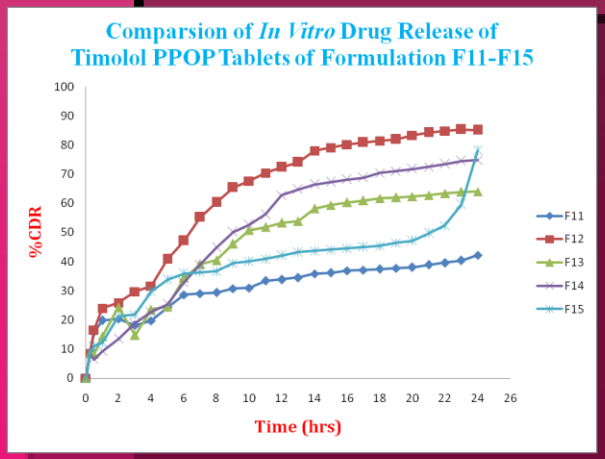


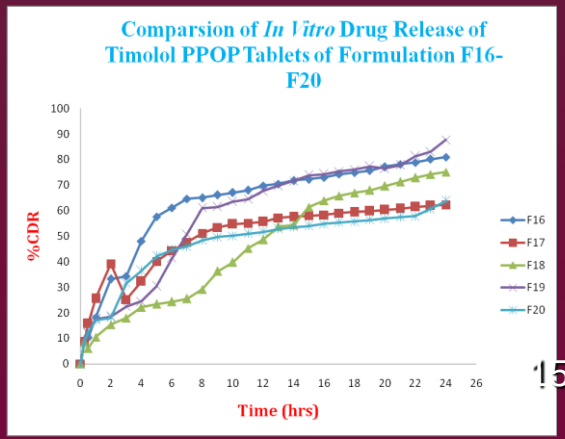
In vitro Drug Release of Timlol melate PPOP Tablets



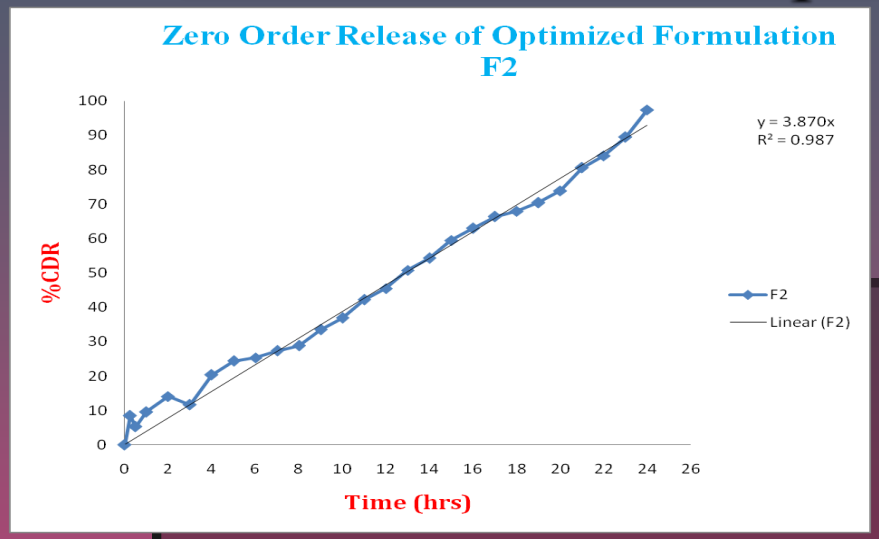


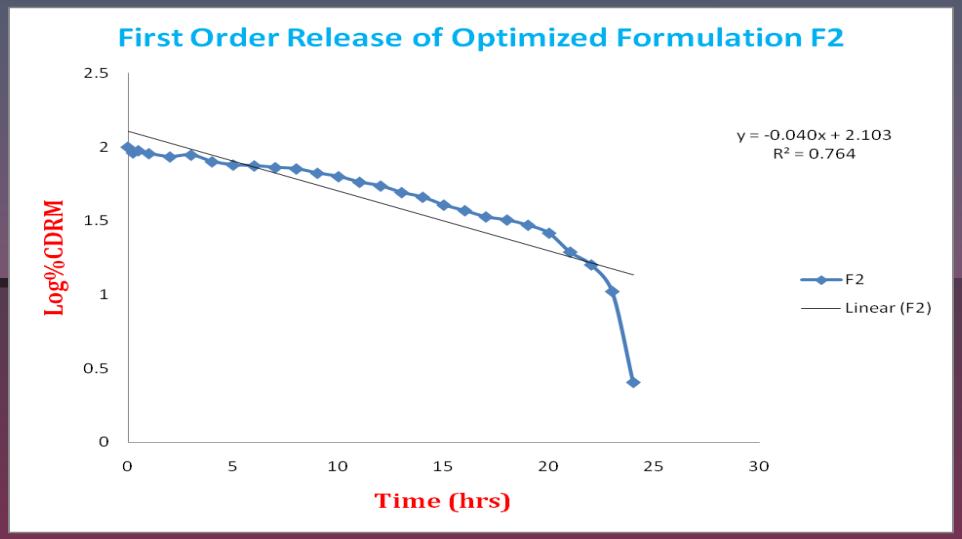


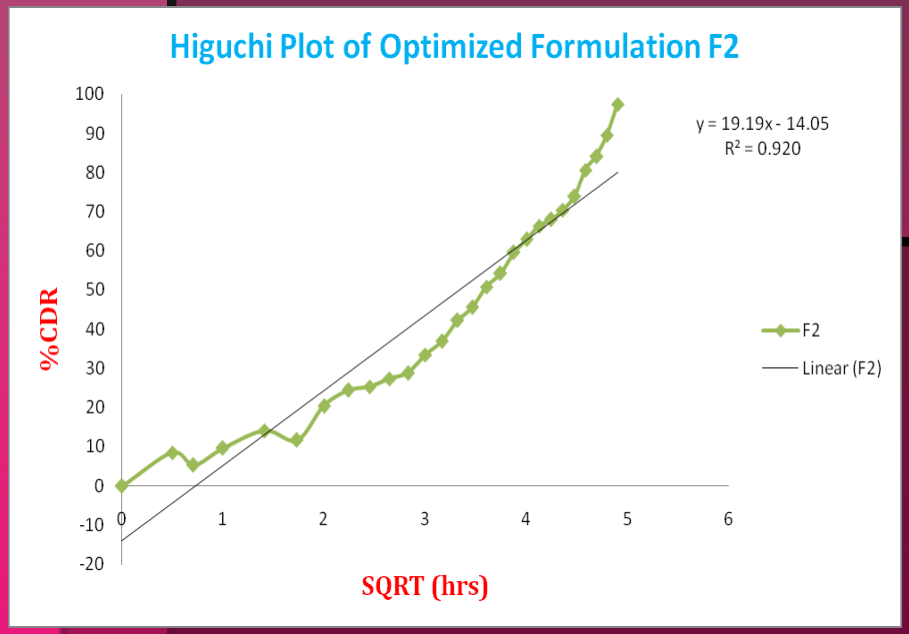


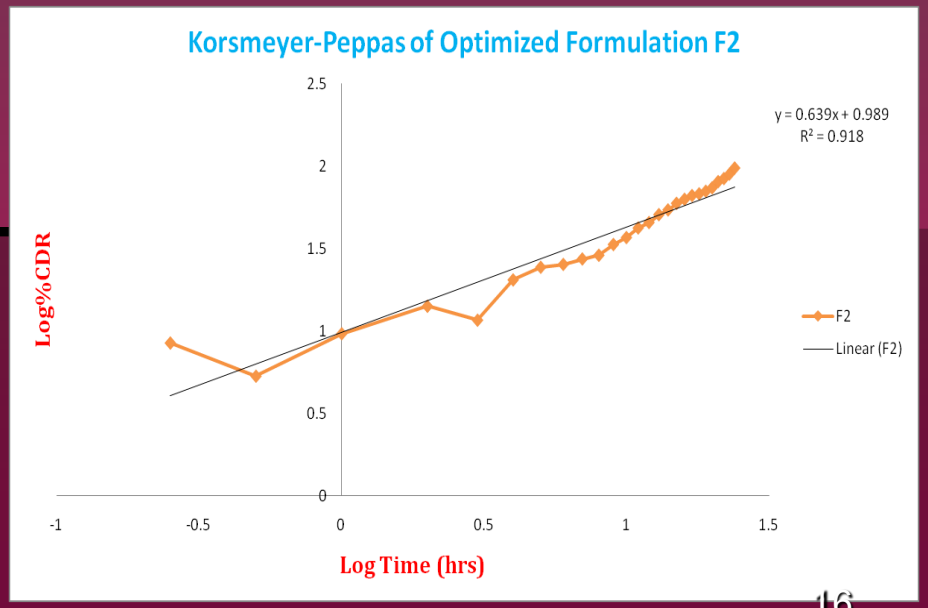


Kinetic Data of Optimized Formulation F2





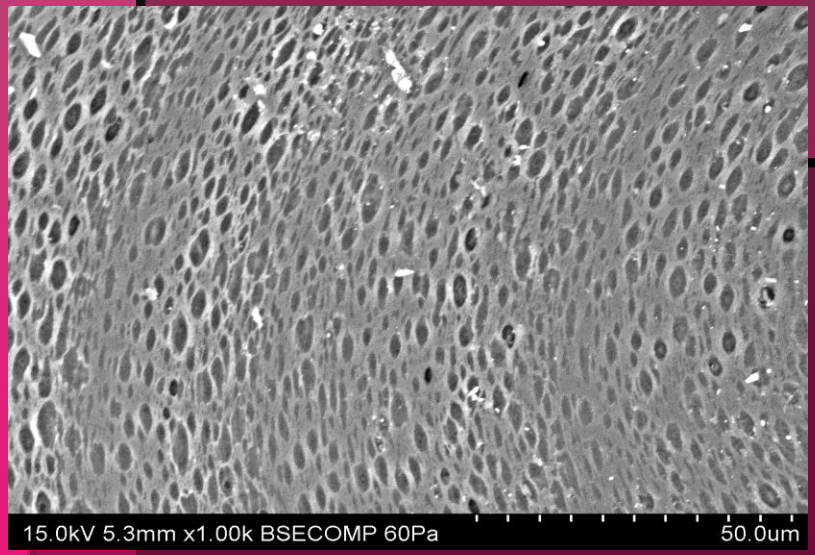


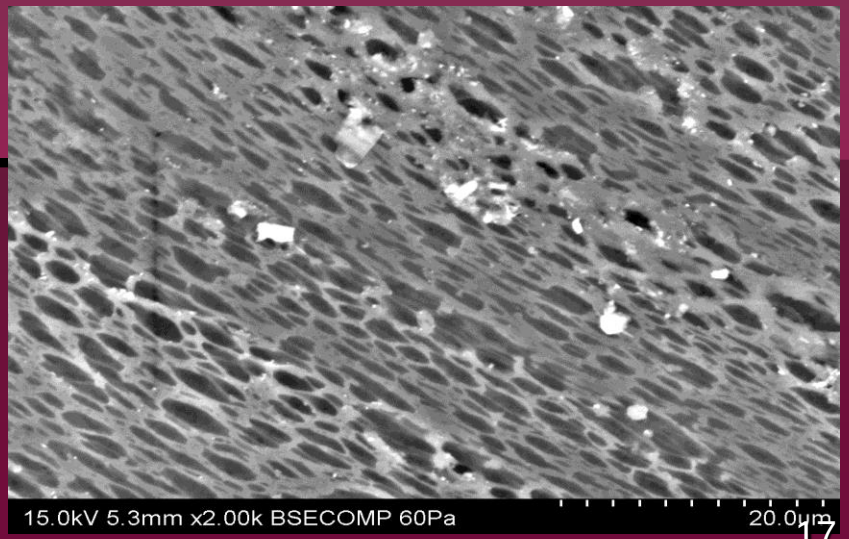


Scanning Electron Micrographs

Optimized Formulation coated Tablet F2 Before Dissolution

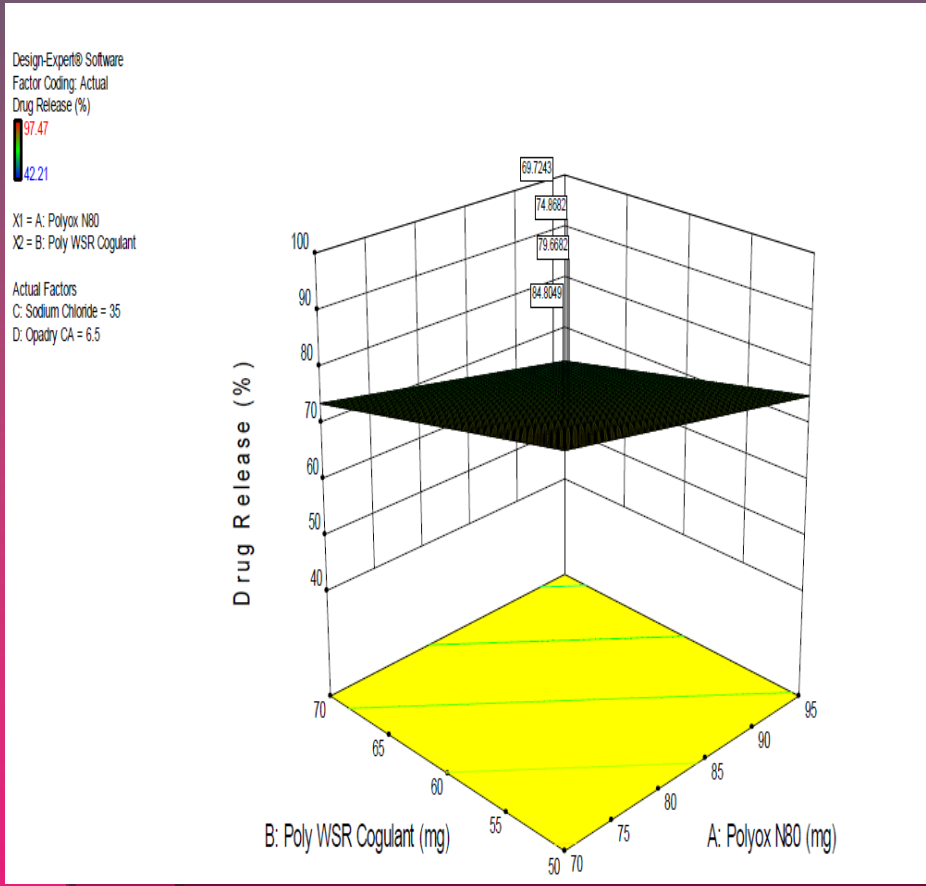
Optimized Formulation coated F2 After Dissolution (Tablet Shell)



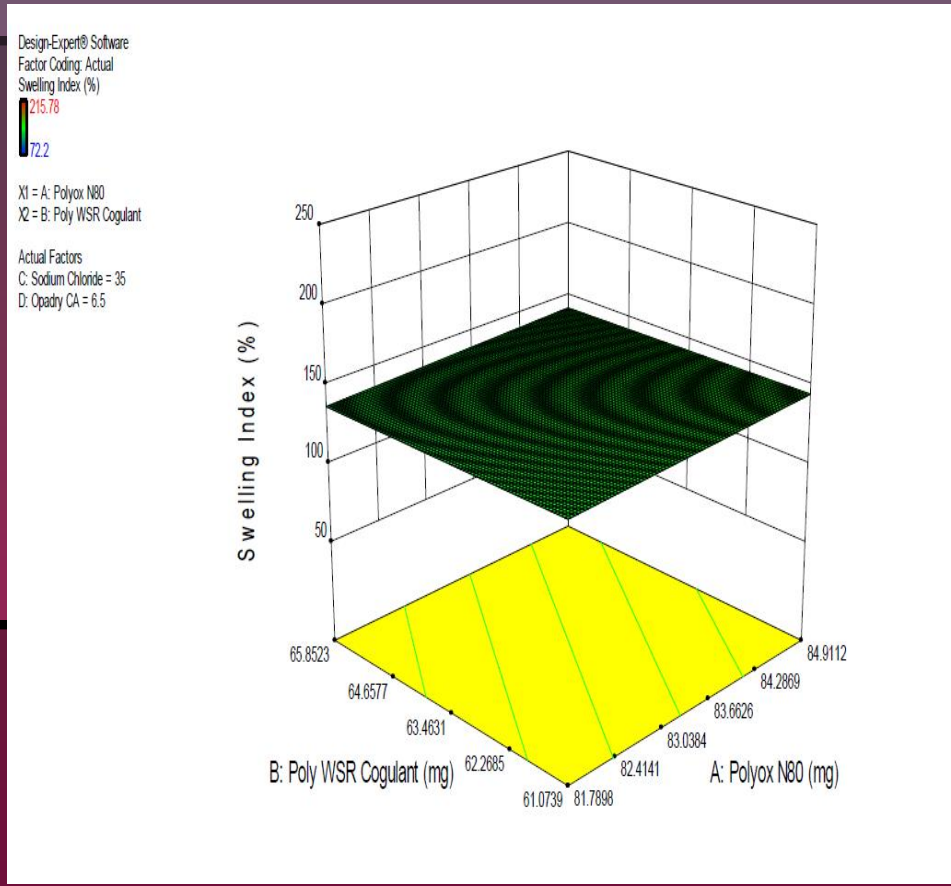


RESPONSE SURFACE CENTRAL COMPOSITE DESIGN GRAPHS

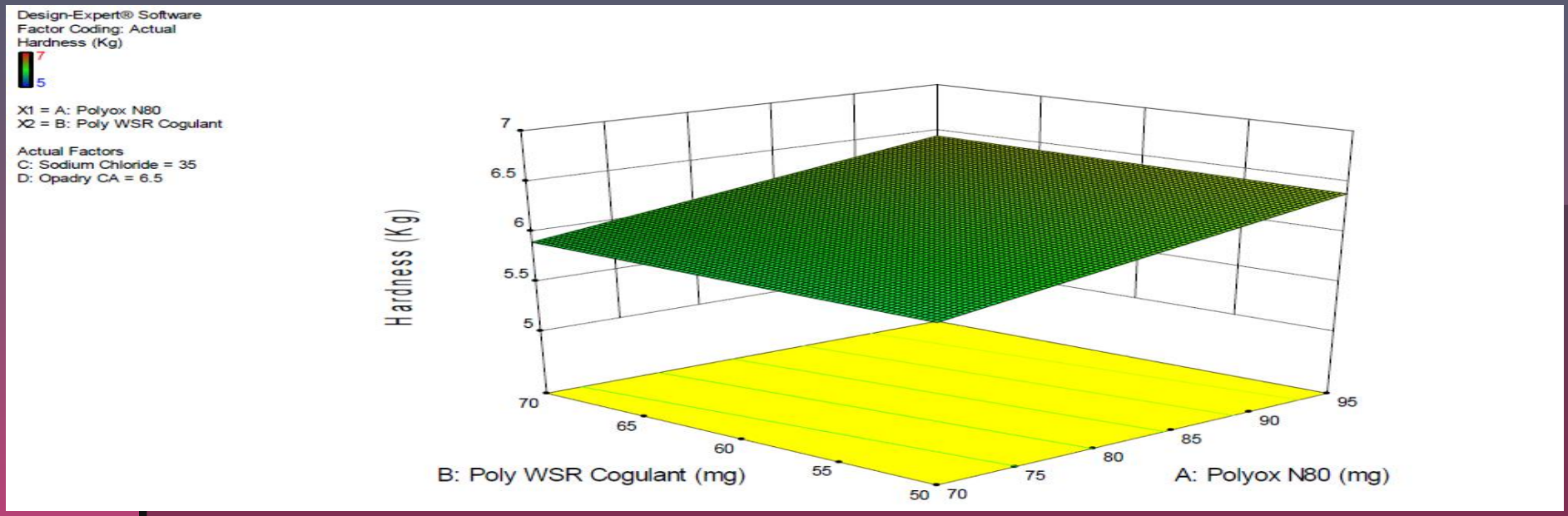
In Vitro Drug Release of Timolol Maleate Bi-layer Push Pull Osmotic Tablet System (PPOP)



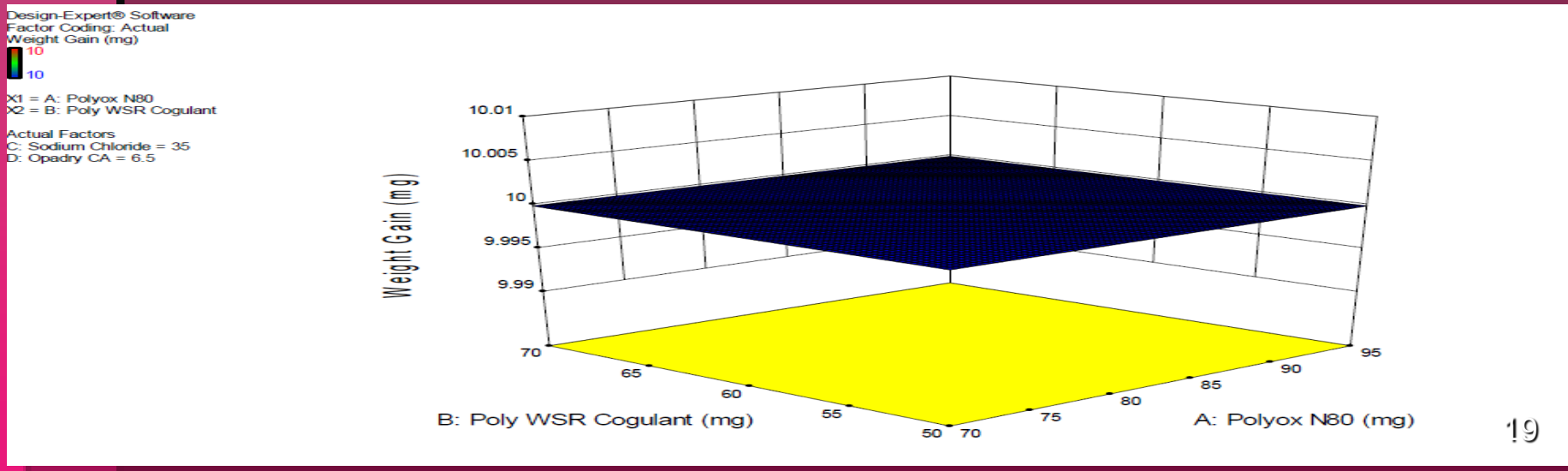
% Swelling Index of Timolol Maleate Bi-layer Push Pull Osmotic Tablet System (PPOP)



Hardness of Timolol Maleate Bi-layer Push Pull Osmotic Tablet System (PPOP)



% Weight Gain of Timolol Maleate Bi-layer Push Pull Osmotic Tablet System (PPOP)



Conclusion

- Based upon the above study, it can be concluded that PPOP tablets have been formulated and Designed Successfully.
- Formulations were sucessfully designed by using Design Expert software by using Response Surface Method & d-Optimaility .
- PPOP Bi-layer Tablets of all the designed Formulations were compressed and pre-compression parameters and post-compression parameters were evaluated .
- Finally the extended release of Timlol Maleate by osmotic technology was achieved by designing the formulations in such a way by varying proportions of polymer and osmogen concentrations.

- All the formualtions were coated by a semipremable membrane by opadry CA with varying Concentration of coating solutions.
- Compatbility of drug and other excipients have been studied by using FTIR and DSC Reports.
- Among all the batches of prepared PPOP tablets, F2 formulation, F8 showed better release of Timlol Maleate from Bi-layer tablets of 97.47 % and all the Pre-compression and Post-compression parameters are also within the limit as per pharmacoepial standards.
- The accelerated stability study of Formulation F2, was studied as per ICH guide lines, by maintaing prescribed temperature and relative humidity conditions in the humidity chamber.

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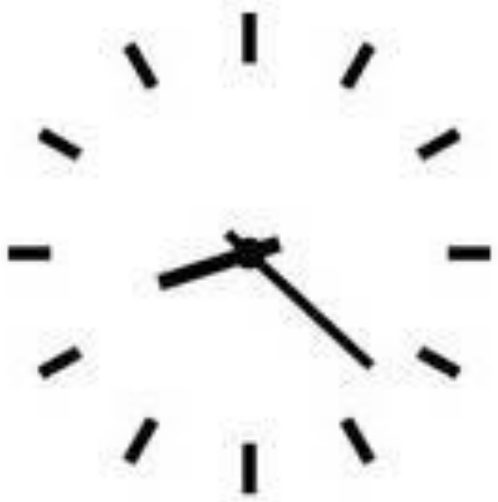

Q & A time


THANK
YOU!