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# FORMULATION AND EVALUATION OF FAST DISSOLVING SUBLINGUAL FILM OF ANTIHISTAMINE DRUG

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***ABSTARCT***
***Oral routes are most usually favored course for delivering drug. Most basic oral dosage structures are tablet and capsules. However, numerous patients, for example, geriatric, pediatric and dysphasic patients discover hard to swallow ordinary tablet and case. To conquer different issues identified with gulping, Fast dissolving Tablets (FDTs) were planned in mid nineteenth century and consequently further progression has prompted improvement of Fast Dissolving Oral Films (FDOFs). In the ongoing years, huge numbers of the drug bunches are zeroing in their examination on rapid dissolving innovation. Among the plenty of roads investigated for rapid drug delivering product, FDOFs innovation is increasing a lot of consideration. These are solid dosage structures, which crumble or dissolve inside 1 min when put in the mouth without drinking water or rumination. This innovation has been utilized for neighborhood activity just as rapid delivery products. The fast dissolving oral films are planned utilizing different Active drug fixings (API), film forming polymers, plasticizer, flavors, colors and sweeteners. At first FDOFs are up to breath strips, dessert and oral consideration markets. In any case, presently it turned into a novel and generally acknowledged innovation for delivering OTC and professionally prescribed medication as well.***
***Keywords: Active drug fixings, oral deteriorating tablet, Promethazine Hydrochloride***

## INTRODUCTION

Oral route is the most favored course for the conveyance of the drugs till date as it bears different points of interest over the other course of drug organization, yet oral drug conveyance frameworks actually need a few headways to be made on account of their a few disadvantages identified with specific class of patients which incorporates geriatric, pediatric and dysphasic patients related with numerous ailments as they experience issues in gulping or biting solid dosage structures. Numerous pediatric and geriatric patients are reluctant to take solid arrangements because of dread of stifling. Indeed, even with fast dissolving tablets there is a dread of stifling because of its tablet type appearance. One examination indicated that 36% of 1776 patients experienced trouble in gulping tablets. The most widely recognized protest was tablet size, trailed by surface

structure and taste. The issue of gulping tablets was more apparent in geriatric and pediatric patients, just as voyaging patients who might not have prepared admittance to water. In this way, fast-dissolving drug-conveyance frameworks appeared in the last part of the 1970's as an option in contrast to tablets, capsules and syrups for pediatric and geriatric patients who experience challenges in gulping customary oral solid-dosage structures. These frameworks comprise of the solid dosage shapes that break down and dissolve rapidly in the oral pit without the organization of water. Innovative work in the oral drug conveyance section has prompted progress of dosage structures from basic traditional tablets or capsules to altered delivery tablets or capsules to oral deteriorating tablet (ODT) to wafer to the ongoing advancement of oral fast dissolving films (OFDFs). Among the plenty of roads investigated for the rapid drug delivering products, oral strip innovation is increasing a lot of consideration. Orally fast-dissolving film is new drug conveyance framework for the oral conveyance of the drugs. It was created based on innovation of the transdermal fix. The conveyance framework comprises of a dainty oral strip, which is essentially positioned on the patient's tongue or any oral mucosal tissue, in a flash wet by salivation the film rapidly hydrates and follows onto the site of use. It at that point rapidly crumbles and dissolves to deliver the medication for oromucosal and intragastric ingestion. Innovation Catalysts conjectures the market for drug products in oral flimsy film details was esteemed of $500 million of every 2007 and could reach $2 billion out of 2012. In view of upward worldwide development patterns of the previous decade, the fast dissolving dosage market could create incomes of $13 billion by 2015.

Fast Drug Delivery Systems are rapidly picking up enthusiasm for the drug business. These frameworks either dissolve or deteriorate by and large inside a moment without requiring water or biting. These frameworks offer prevalent clinical profiles with potentional oro mucosal retention in this manner expanding the drug bioavailability as for oral organization. As of late flimsy films have been proposed which rapidly dissolves or deteriorates into buccal pit. Mouth dissolving films are novel dosage shapes that crumble or dissolve in the oral cavity. These are ultra slender postage stamp size with a functioning specialist or drug excipients. These dosage structures are put on the tongue or any mucosal tissue. At the point when wet with salivation, the films rapidly hydrates and holds fast on to the site of use. It rapidly dissolves or deteriorates to deliver the medication for mucosal ingestion or with alteration, takes into consideration oral GIT assimilation with brisk dissolving properties. A significant advantage of these dosage structures is exact dosing when contrasted with fluid dosage structure, no water is required and there is no dread of gagging when contrasted with tablets and capsules. Subsequent to deteriorating in the mouth, upgraded the clinical impact of drug through pre-gastric ingestion from mouth pharynx and throat as the spit goes down into the stomach. In such cases, bioavailability of drug is essentially more noteworthy than those saw from customary tablet dosage structure. All the more as of late, Fast-dissolving buccal film drug delivery frameworks have rapidly picked up acknowledgment as a significant better approach for directing drugs. They are normally utilized for drug and nutraceuticals products. It is the freshest boondocks in drug delivery innovation that gives a helpful methods for taking medications and enhancements. Fast dissolving films are likewise material when neighborhood activity in the mouth is attractive, for example, nearby sedative for toothaches, oral ulcers, mouth blisters, or teething.

Oral route is the most favored course of organization for fundamental impact. About 60% of all plans are of solid dosage structure. Tablet is the most favored dosage structure because of simplicity of transportation, assembling and more patient consistence. By and large pediatric geriatric and taboo patients experience challenges in gulping the traditional tablet. To defeat this issue a novel detailing was created .for example oral fast dissolving films.FDF is readied utilizing hydrophilic polymers that rapidly dissolves on the tongue or buccal hole, delivering the drug to the fundamental flow by means of buccal mucosa. The fast dissolving drug delivery framework are uniquely intended for the drugs which have broad first pass digestion and have low portion, for the improvement of bioavailability.

**Special features of Mouth dissolving films**

Excellent mucoadhesion,
Available in various size and shape
Unobstructive
Thin elegant film
Rapid release
Fast disintegration

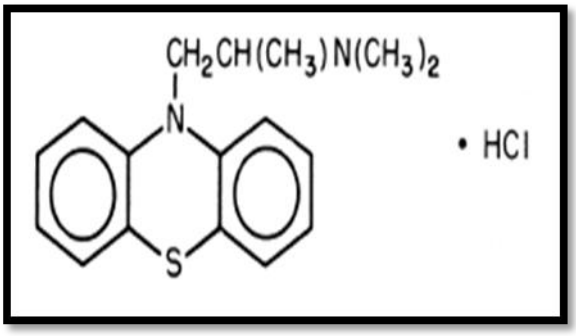
## LITERATURE REVIEW

Abraham Linku et.al.,(2018) recommended that the point of present work was the improvement of fast dissolving oral film of Loratadine to beat the constraints of current routes of organization, to give prompt activity and increment the patient consistence. To improve the bioavailability of the drug, fast dissolving oral film were figured utilizing various evaluations of Hydroxy Propyl Methyl Cellulose(HPMC) and different plasticizers like Polyethylene Glycol(PEG) 400, glycerol, Propylene glycol(PG) by dissolvable projecting technique. The defined films were assessed for film thickness, surface pH, collapsing perseverance, weight variety, % dampness misfortune, exvivo saturation study, rigidity, % stretching, drug content consistency, in vitro disintegration examines, in vitro breaking down test and in vivo examination. The streamlined definition (F9) containing HPMC E5 and glycerol indicated least deterioration time (10.5 s), most elevated in vitro disintegration (92.5%) and acceptable security. Ex vivo penetration investigation of improved definition indicated a drug arrival of 80.6% inside 10 min. The milk prompted leucocytosis inrat demonstrated that fast dissolving oral films of Loratadine created a faster beginning of activity contrasted with the customary tablets. These discoveries propose that fast dissolving oral film of Loratadine could be possibly helpful for treatment of hypersensitivity where brisk beginning of activity is required.
Parul Saini et.al.,(2012) demonstrated that the Oral fast breaking down films (OFDF) is a developing innovation brings out "definitions taken without water" with snappy beginning of activity and improved patient consistence. Oral films give better drug usage in by-passing the primary pass digestion, upgrade drug bioavailability, cover the severe taste of the drug and needn't bother with water to swallow. OFDF plans are appropriate for hack, cold cures, sore throat, allergenic conditions, sickness, agony and CNS issues. Multivitamins, caffeine strips, wheezing guide and tranquilizers are additionally material for consolidation in the oral films. The significant imperatives of OFDF are restricted drug watery dissolvability, helpless penetrability and its high portion. Present article diagram the progression in the oral dosage structures, application, plan thought, technique for arrangement, assessment, showcased product and licensed advancements of oral fast breaking down films.

## DRUG PROFILE

### PROMETHAZINE HYDROCHLORIDE

**Chemical structure:**



**Molecular formula** : C17H20N2S•HCl
**Molecular weight** : 320.88.
**Chemical name** : (RS)-N, N-dimethyl-1-(10H-phenothiazin-10-yl) propan-2- amine hydrochloride.
**Solubility** : Promethazine HCl as the hydrochloride salt is freely soluble in water and somewhat soluble in alcohol.
**Melting point** : 220-222ºC.
**$P^{ka}$ and pH** : 9.1 and 5.8.
**Log P** : 4.7
**Dose** : 10 mg to 25 mg and maximum dose per day is 25 mg.
**Storage** : Store in a cool dry place, away from direct heat and light.
**Beer's Range** : 2-12µg/ml.

## PROPOSED METHODLOGY

### Materials and Methods

Promethazine Hydrochloride was acquired as sample from Syncom Healthcare Limited Indore, Madhya Pradesh. HPMC E15, PEG400, sucrose, citrus extract, Titanium dioxide, strawberry and sodium lauryl sulfate, microcrystalline cellulose utilized were of expository evaluation.

### Preparation of Fast Dissolving Oral Films:

The fast dissolving oral film of promethazine hydrochloride were set up by the dissolvable projecting method utilizing HPMC E-15 as a film forming polymer and PEG as a plasticizer. SLS and MCC were utilized as a surfactant. Citrus extract as salivation animating specialist. Sucrose as an improving specialist and strawberry as an enhancing operator. The details were readied . The hydrophilic polymers in particular hydroxy propyl Methyl cellulose (HPMC) and Polyethylene glycol (PEG) were precisely gauged and dissolved in 10ml hot refined water and was blended for 3 hours. In second arrangement Drug (dissolves in ethanol and chloroform 1:1 blend) and different fixings Titanium dioxide, SLS/MCC (as indicated by detailing) blended. Sucrose and citrus extract was dissolving in 15 ml refined water steady mixing with an attractive stirrer. The third arrangement was set up by mixing second arrangement in first arrangement. Include strawberry flavor in third arrangement and saved for 3hours to eliminate air bubble and the resultant homogeneous arrangement was filled a petri dish. At that point the films were dried in a broiler at 550C for 24 h. The dried films were enclosed by a spread paper and cut into 4x2 cm2 zone, secured with an aluminum foil and kept in a desiccators. Chosen films were exposed to various assessment boundaries.

### Formulation of Promethazine Hydrochloride Oral Film:

### Evaluation of Fast Dissolving Oral Films:

### Transparency:

Transparency was assessed by visual appearance of oral film and ordered in different levels, for example, best, great, medium, terrible for transparency.

### Film Weight variation:

For evalution of film weight four films of every formulation were taken and weighed exclusively. The normal weight were determined and revealed.

### Thickness:

For evalution of film thickness three films of every formulation were taken and the film thickness was estimated utilizing micrometer screw measure at three better places and the mean thickness of films were determined and detailed.

**Tensile strength:**

For evalution of film tensile quality (TS) of every formulation were taken and compute elasticity with the assistance of equation:

Tensile strength= load at failure ×100 Film
Thickness ×Film Width

**Folding Endurance:**

Folding endurance is estimated by manual continued collapsing of film at same spot till it broke. The quantity of time the film is collapsed without breaking is known as the collapsing continuance esteem. A piece of 4 × 2cm distance across (a zone of 8 cm2) was exposed to collapsing perseverance by collapsing the film at a similar spot over and again a few times until an obvious split was watched, and the normal qualities were determined and announced.

**Surface pH:**

Surface pH of the films was resolved so as to examine the conceivable symptoms because of progress in pH in vivo, since an acidic or basic pH may make disturbance the buccal mucosa. The film was put in a Petri dish and dampened with 1 ml of refined water and saved for 2 h. pH was noted with the terminal of the pH meter. The normal of three conclusions for every formulation was finished.

**Surface texture:**

Surface was assessed by visual appearance of oral film and arranged in smooth to harsh surface demonstrates by numerical + sign.

**Moisture absorption:**

The film sample is gauged and set on a pre-gauged hardened steel wire work. The wire work is then lowered in a petridish containing 20 ml refined water. Increment in weight of the film is resolved at ordinary time stretches (20 min) until a steady weight is gotten the hydration proportion of the film is determined and normal dampness retention is determined and detailed.

**Hydration ratio= Wt-W0×100/W0**

Where Wt = weight of film at time t and W0 = weight of film at zero time.

**Moisture loss:**

The percent moisture misfortune was dictated by setting arranged film in desiccators containing anhydrous calcium chloride. Following three days, the film was taken and rechecked. Normal percent moisture misfortune was determined.

**Moisture loss=W0/W0-Wt×100**

Where W0= initial weight Wt = final weight

**Drug content**:

A specified area of strip (4cm×2cm) was dissolved in 200 ml water in volumetric cup and shaken ceaselessly for 20 min. Channel the arrangement by 0.45µm membrane filter paper. After filtration, 1ml of arrangement was pulled back from the arrangement and weakened up to10ml with water. The absorbance of the arrangement was estimated at 249.60 nm and fixation was determined and decided the drug content.

**In vitro drug release test**:

Dissolution profile of promethazine hydrochloride was done in a measuring glass containing 20 ml of the mimicked salivary liquid pH 6.8 as a dissolution medium, kept up at 37±0.20°C. The medium was mixed at 100 rpm with attractive stirrer. Aliquots of the medium were pulled back at normal time period min and a similar sum was supplanted with new medium. Samples were investigated for aggregate rate drug discharge

by Shimadzu UV-noticeable spectro photometry at 249.60 nm. Three preliminaries were done for all the samples and normal was taken.

In vitro release of drug from all formulations was resolved utilizing USP contraption type II (Paddle strategy). The accompanying conditions were followed to examine the in-vitro dissolution investigation of promethazine hydrochloride mouth dissolving film -

1. Dissolution apparatus: USP Type II (Paddle method)
2. Volume of dissolution medium: 800 ml
3. Temperature: 37±0.200C
4. Dissolution medium: simulated salivary fluid (pH6.8)
5. Sampling interval: 5min
6. Quantity of sample withdrawn: 20ml

## RESULTS AND DISCUSSION

### Determination of solubility:

Promethazine HCl was found to be freely soluble in water and alcohol.

### Determination of melting point:

The melting point of Promethazine HCl was found to be in the range of 220ºC.

### Determination of λmax:

Wavelength of maximum absorption of Promethazine HCl in phosphate buffer pH6.8.

| SR.No. | Solvent | λmax |
|---|---|---|
| 1 | Phosphate buffrer pH 6.8 | 249.60 |

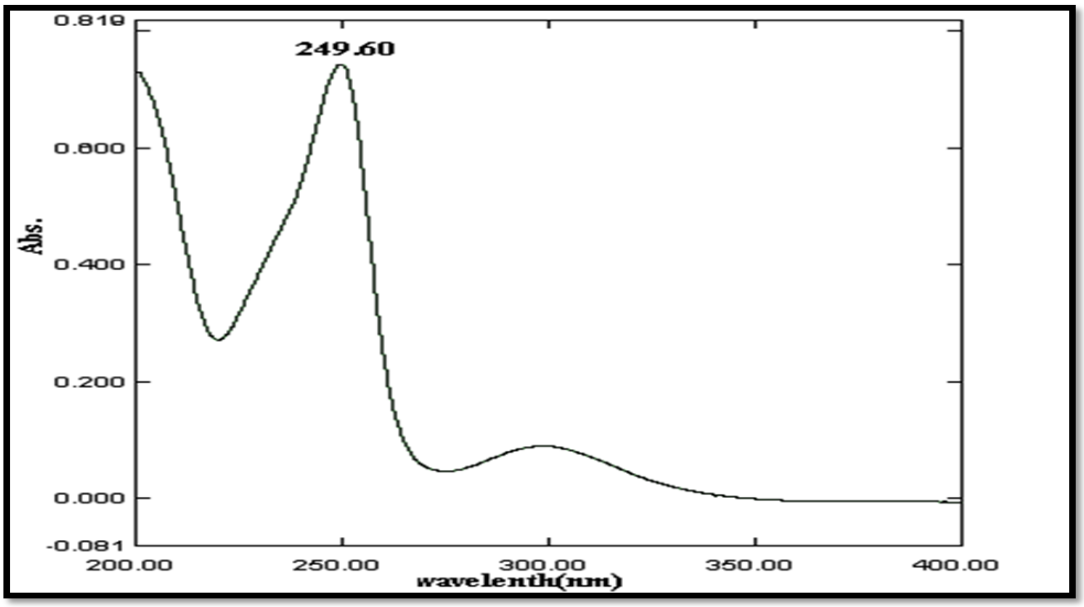



**Figure 1:**UV spectra of Promethazine HCl in phosphate buffer pH 6.8

**Drug–polymer compatibility by FTIR studies:**

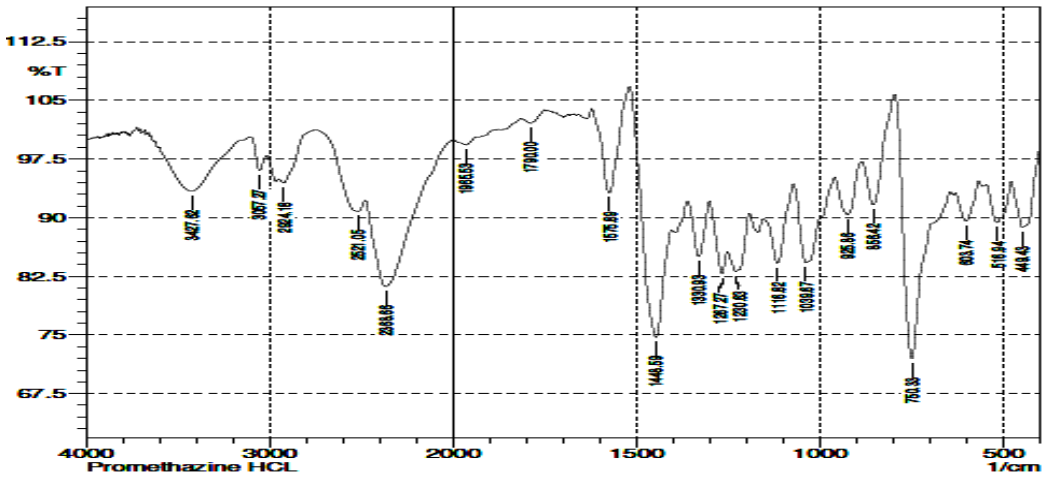



**Figure 2:** IR spectra of Promethazine HCl

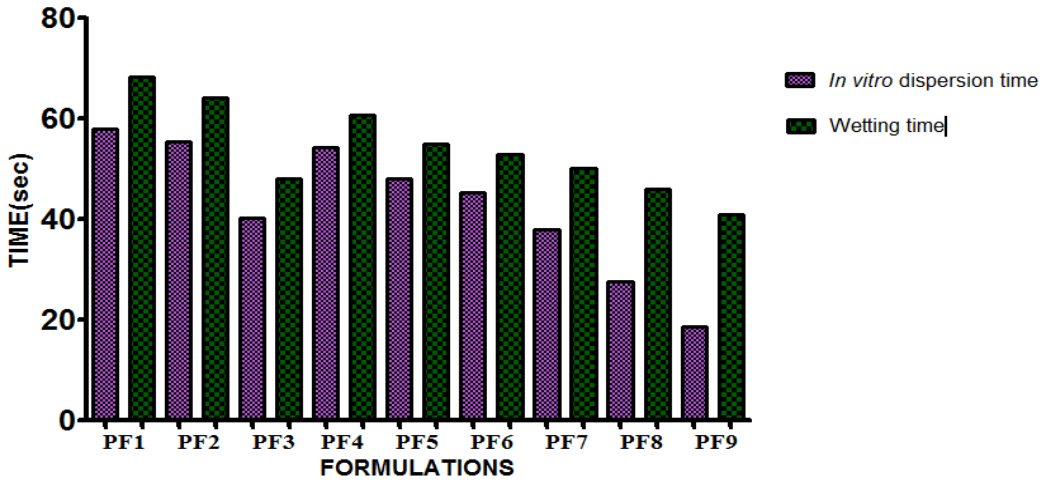



**Figure 3:** Comparison between *in vitro* dispersion time and wetting time of Promethazine HCl Tablets

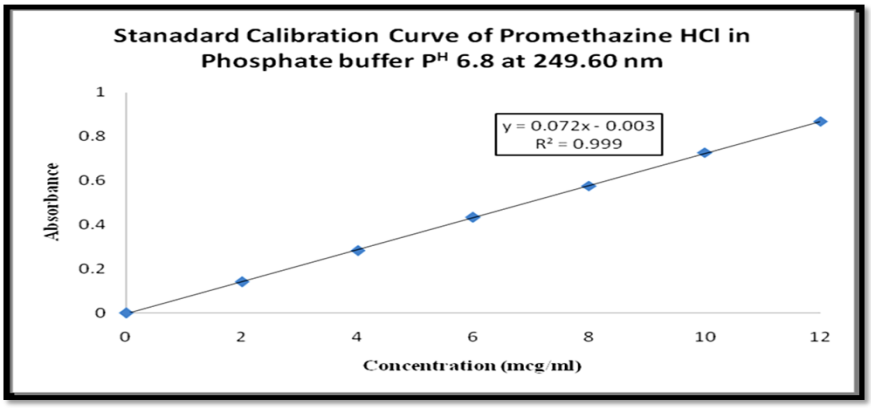



**Figure 4:** Standard calibration curve of Promethazine HCl in phosphate buffer pH at 249.60nm

**Table No.1:** Data for% drug content of Promethazine HCl tablets

| Formulation code | % Drug contest |
|---|---|
| PF 1 | 98.21±0.66 |
| PF 2 | 98.21±0.66 |
| PF 3 | 96.78±0.86 |
| PF 4 | 98.55±0.76 |
| PF 5 | 98.73 ± 1.10b |
| PF 6 | 98.22 ± 0.38 |
| PF 7 | 99.28±0.28 |
| PF 8 | 98.91±0.81 |
| PF 9 | 99.71±0.16 |

**Table No.2:** Characterization of the marketed tablets of Promethazine HCL (Phenargen)

| SR. No. | Evaluation Parameter | Observations |
|---|---|---|
| 1 | Thickness* | 2.70±0.05 mm |
| 2 | Hardness* | 4.3±1.23 kg/cm$^2$ |
| 3 | Friability* | 0.35±0.03 % |
| 4 | Weight variation | 151±2.49 mg |
| 5 | % Drug content* | 98.20±1.79% |
| 6 | % Cumulative drug release | 93.48 ( 1 hour) |

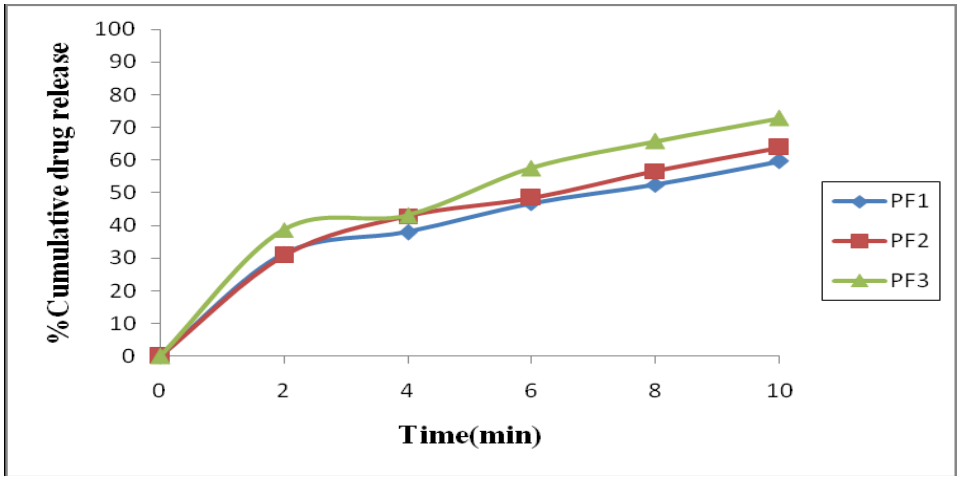



**Figure 5:** *In* vitro drug release profile of Promethazine HCl tablets containing SSG

## CONCLUSION

The present study demonstrated that SLS and MCC Surfactant can be used for the preparation of Promethazine Hydrochloride fast dissolving film. The most important advantage of the fast dissolving films is that it contains a lower drug dose, adequate for therapeutic effect. Moreover, this film is very contented because it is non-irritant and self administration is possible. This study shows that it is possible to formulation of different surfactant with different concentration were used in Promethazine Hydrochloride drug fast dissolving film formulation. The intention of obtaining better therapeutic efficiencywith increasing bioavailability and improving patient compliance. Fast dissolving Films were found to be satisfactory when evaluated for thickness, weight uniformity, in-vitro drug release, folding endurance, drug content and disintegration time. The surface pH of all the films was found to be neutral. The pre-compression parameters like bulk density, tapped density, Carr's 'index and angle of repose were determined. The final formulation showed acceptable flow properties. The post-compression parameters like the thickness, hardness, friability and in vitro dispersion time, wetting time, water absorption ratio and in vitro drug release were carried out and the values were found to be within IP, BP limits. Hence based on the formulation development and their results, direct compression method is more suitable for Promethazine HCl rapid dissolving tablets in terms of palatability, physical and chemical properties better with reference product.

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