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# PREPARATION AND EVALUATION OF FAST DISSOLVING ORAL FILM OF PERINDOPRIL ERBUMINE TABLETS

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## ABSTRACT

**Perindopril Erbumine** Tablets contain the active substance perindopril erbumine which belongs to a group of medicines known as angiotensin converting enzyme (ACE) inhibitors. These work by making your blood vessels wider, which makes it easier for your heart to pump blood through them. Fast dissolving oral films are useful in patients such as paediatric, geriatric, bedridden or developmentally disabled who face difficulty in swallowing conventional tablets or capsules and liquid orals or syrups leading to ineffective therapy. The delivery system consists of a very thin oral strip, which is simply placed on the patient's tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. The present study was aimed to formulate fast dissolving oral films to enhance bioavailability and avoid pre systemic metabolism. The key is to develop successful oral film by solvent casting method and selected the right compatible excipients using FTIR studies. Oral film was fabricated using HPLC E5 and HEC polymer. The prepared films were evaluated for Organoleptic evaluations, film weight, thickness, folding endurance, tensile strength, drug content uniformity of films, surface pH, disintegration time and in-vitro dissolution studies. The formulation F5 has disintegration time of 7 seconds and is more promising and showed drug release of 98% after 5 minutes; hence formulation F5 was selected as best formulation.

## INTRODUCTION

(perindopril erbumine) Tablets is the tert-butylamine salt of perindopril, the ethyl ester of a non-sulfhydryl angiotensin-converting enzyme (ACE) inhibitor. Perindopril is the free acid form of perindopril erbumine, is a pro-drug and metabolized *in vivo* by hydrolysis of the ester group to form perindoprilat, the biologically active metabolite. ACEON® Tablets is available in 2 mg, 4 mg and 8 mg strengths for oral administration. The mechanism through which perindoprilat lowers blood pressure is believed to be primarily inhibition of ACE activity. ACE is a peptidyl dipeptidase that catalyzes conversion of the inactive decapeptide, angiotensin I, to the vasoconstrictor, angiotensin II. Angiotensin II is a potent peripheral vasoconstrictor, which stimulates aldosterone secretion by the adrenal cortex, and provides negative feedback on renin secretion. Inhibition of ACE results in decreased plasma angiotensin II, leading to decreased vasoconstriction, increased plasma renin activity and decreased aldosterone secretion.

An attempt has been made for the preparation of fast dissolving oral film of perindopril with an aim to provide the following advantages. Availability of larger surface area that leads to rapid disintegrating and dissolution in the oral cavity and promote the systemic absorption of APIs with no need of water or a spoon for administration and without chewing. The drug enters the systemic circulation with reduced hepatic first pass effect and provide rapid onset of action. Delivery can also be terminated relatively easily if required. Site specific action and local action can be acheived. Good mouth feel With the help of Mouth dissolving film drug delivery system. Those drugs can be given to the patients that are not crushed and not injected by patient fast dissolving oral films are best choice. Enhanced oral bioavailability of molecules that undergo first pass effect can be achevied. Mouth Dissolving Films are typically the size of a postage stamp and disintegrate on a patient's tongue in a matter of seconds for the rapid release of one or more APIs.

## MEHODOLOGY

**Materials used in the present work.**

| S.no | Ingrediens | Suppliers |
|---|---|---|
| 1 | Perindopril | Parachem |
| 2 | HPMC | Parachem |
| 3 | PEG | Parachem |
| 4 | Chitosan | Sisco research laboratories |
| 5 | Propylene glycol | Scientific fischer |
| 6 | Sucrose | Scienific fischer |
| 7 | Methanol | Merck |

**Instruments used in the present work**

| S.no | Name of instrument | Manufacturing company |
|---|---|---|
| 1 | Digital balance | Shimadzu |
| 2 | Dissolution apparatus | Lab India |
| 3 | UV-VIS Spectro photometer | Lab India |
| 4 | pH meter | Lab India |
| 5 | FT-IR Spectrophotometer | Shimadzu |
| 6 | Magnetic stirrer | Remi equipments p5rvt limited |
| 7 | Stability chamber | Labline |

**Preformulation Studies**

Preformulation testing is an investigation of physical and chemical properties of drug substances alone and combined with excepients. It is the first step in the rational development of dosage form.

**FT-Infrared spectroscopic sudies**

One of the requirements for the selection of suitable exepients or carrier for pharmaceutical formulation is its compatability. Therefore in the present work a study was carried outinfrared spectrophotometer to find out if thereis any possible chemical ineraction of aenolol with sodium sarch glycolate, HPMC, lactose, Magnesium stearate and talc.

**Procedure**

Weighed amont of drug (3mg) was mixed with 100mg of potassium bromide(dried at40-50$^0$C**).** The mixture was taken and compressed under 10-ton pressure in a hydraulic press to form a pellet. The pellet was scanned in IR spectrophotometer.

**COMPOSITION OF FORMULATIONS**

| Formulation code | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 | F11 | F12 | F13 | F14 | F15 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Perindopril(mg)** | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| **HPMC (mg)** | 250 | 250 | 350 | 350 | 450 | 450 | 250 | 250 | 350 | 350 | 450 | 450 | 250 | 350 | 450 |
| **Chitosan(mg)** | 125 | 250 | 175 | 350 | 225 | 450 | - | - | - | - | - | - | - | - | - |
| **PEG(mg)** | - | - | - | - | - | - | 125 | 250 | 175 | 350 | 225 | 450 | - | - | - |
| **Methanol(ml)** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| **Propyleneglycol(ml)** | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| **Sucrose (mg)** | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |

**Procedure for construction of standard curve**

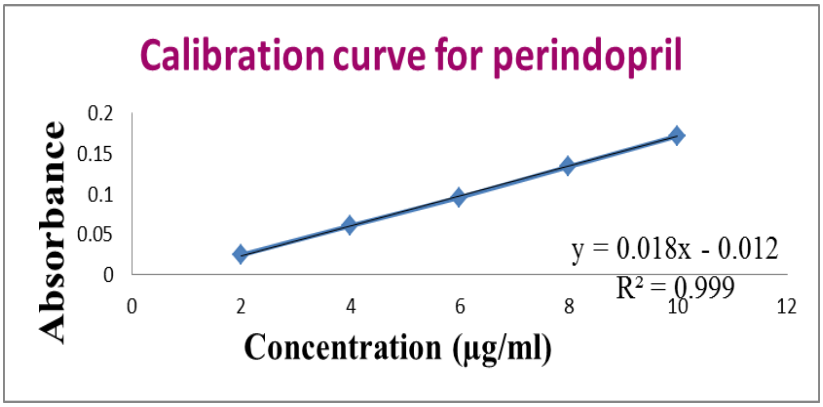
Standard stock solution of perindopril was prepared by dissolving 10 mg of drug in 10 ml of water to get concentration of 1000µg/ml. 10 m1 of standard stock solution of perindopril was then diluted with water to get working standard solution of 100µg/ml. From the resultant

solution 2, 4, 6, 8, 10µg/ml were prepared from the above stock solution. The absorbance was measured at 210nm using distilled water as blank and plotted to get the calibration curve.

**Calibration data for perindopril in water**

| S.no | Concentration (µg/ml) | Absorbance (210 nm) |
|---|---|---|
| 1 | 2(µg/ml) | 0.025 |
| 2 | 4(µg/ml) | 0.061 |
| 3 | 6(µg/ml) | 0.096 |
| 4 | 8(µg/ml) | 0.134 |
| 5 | 10(µg/ml) | 0.174 |

**Calibration curve for perindopril in water**




Slope 0.018

Intercept 0.096

Regression 0.999

**Method of preparation of Fast Dissolving Oal Film[81,82]**

Drug containing fast dissolving fims were fabricated by the solvent casting method. The optimized amount of polymer was dissolved in 5ml of water and stirr continuously for 1 hour using magnetic stirrer. Optimized amount of sweetener, and Plasticizer were dissolved in 95% ethanol and then added to the polymeric solution, Thenthe optimized amount of drug was dissolved in 2ml of water and kept on sonication for proper dispersion. The drug solution was then added to the polymeric solution and stirred for 30 min using magnetic stirrer and was kept in undisturbed condition till the entrapped air bubbles were removed. The above solution was then casted on glass plate and was dried at controlled room temperature (25° - 30°C, 45% RH) as well as at increased temperature (microwave oven). The film took approximately 48 hr to dry at controlled room temperature. The dried film was then carefully removed from the glass plate and was cut into size required fortesting.

## EVALUATION OF THE PREPARED FILM[83-92]

### Film Thickness

As the thickness of film is directly concern with drug content uniformity so it is necessary to ascertain uniformity in the thickness of the film. It can be measured by micrometer screw gauge or calibrated digital Vernier Calipers at different strategic locations. The thickness of each of 10 film of each type of formulation was measured and the average was determined.

### Weight Variation

The mass of the films was determined by using analytical balance**.** When manufacturing the oral films, the film solutions were cast into sheets and then cut into smaller strips of 4 cm2 (2cm×2 cm). Oral films were cut from different sheets and the variability between the respective polymers as well as the variability between the polymers were investigated. The individual weight each of 10 samples of each formulation was determined.

**Hydration Study (water uptake/ swelling study):** The film sample was weighed and placed on a preweighed stainless steel wire mesh. The wiremesh was then submerged in a petridish containing 20 ml distilled water. Increase in weight of the film was determined at regular time intervals until aconstant weight was obtained. The hydration ratio of the film was calculated usingfollowing formula

$$\text{Hydration ratio} = \frac{Wt - W0}{W0}$$

Where Wt = weight of film at time t and

W0 = weight of film at zero time.

### Moisture Loss (Moisture Vapor Transmission)

The percent moisture loss was determined by placing prepared film in desiccators containing anhydrous calcium chloride. After three days, the film was taken and reweighed. The percent moisture loss was calculated using following formula

$$\text{Moisture loss} = \frac{W0}{W0 - Wt} \times 100$$

Where W0= initial weight

Wt = final weight.

**Measurement of Mechanical Properties**

To avoid mechanical failure of the film and to ensure that film can bear the stress during transportation and storage, the following mechanical properties were measured.

**Tensile strength:** Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by the applied load at rupture divided by the cross-sectional area of the strip. It is given by the equation as followes.

$$\text{Tensile strength} = \frac{\text{Load at breakage}}{\text{Strip thickness} \times \text{Strip Width}}$$

The tensile testing gives an indication of the strength and elasticity of the film, reflected by the parameters - tensile strength, elastic modulus, % strain, and load at yield. The type of the polymer is characterized by following table.

**Mechanical Properties of Film**

| Type of polymer | Tensile Strength | Elastic Modulus | % Strain |
|---|---|---|---|
| Soft and Weak | Low | Low | Low |
| Hard and Brittle | Moderate | High | Low |
| Soft and Tough | Moderate | Low | High |
| Hard and Tough | High | High | High |

The mechanical properties of the film gives idea about to what extent the film can withstand the force or stress during processing, packaging, transport and handling. The desirable characteristics of film are moderate tensile strength, low elastic modulus, high % strain and high load at yield. From the above table, the polymer should give soft but tough film.

**Percent Elongation**

When stress is applied, a strip sample stretches and this is referred to as strain. Strain is basically the deformation of strip divided by original dimension of the sample. Generally elongation of strip increases as the plasticizer content increases.

$$\% \text{ Elongation} = \frac{\text{Increase in length} \times 100}{\text{Original length}}$$

**Folding Endurance**

Folding endurance is determined by repeated folding of the strip at the same place till the strip breaks. The number of times the film is folded without breaking is computed as the folding endurance value.

**Surface pH**

The surface pH of fast dissolving oral thin films was determined in order to investigate the possibility of any side effects *in vivo*. As an acidic or alkaline pH may cause irritation to the oral mucosa, it was determined to keep the surface pH as close to neutral as possible. A combined pH electrode was used for this purpose. Oral strip was slightly wet with the help of water. The pH was measured by bringing the electrode in contact with the surface of the film.

**Compatibility studies**

The drug-polymer compatibility was confirmed by taking IR spectrum and DSC thermogram of drug, polymer and physical mixture of drug-polymer.

**Drug Content and Content Uniformity**

The drug content and content uniformity test was performed to ensure uniform distribution of drug. This is determined by any standard assay method described for the particular API in any of the standard pharmacopoeia. Content uniformity is determined by estimating the API content in individual strip. Limit of content uniformity is 85–115 percent.

**In vitro Disintegration and Dissolution Time**

The disintegration time is the time when a film starts to break or disintegrate. Disintegration of orally fast dissolving films requires USP disintegration apparatus. Disintegration time will vary depending on the formulation but typically the disintegration range from 5 to 30 seconds. Although, no official guidance is available for oral fast disintegrating films strips. The dissolution time is the time when the film completely dissolves.

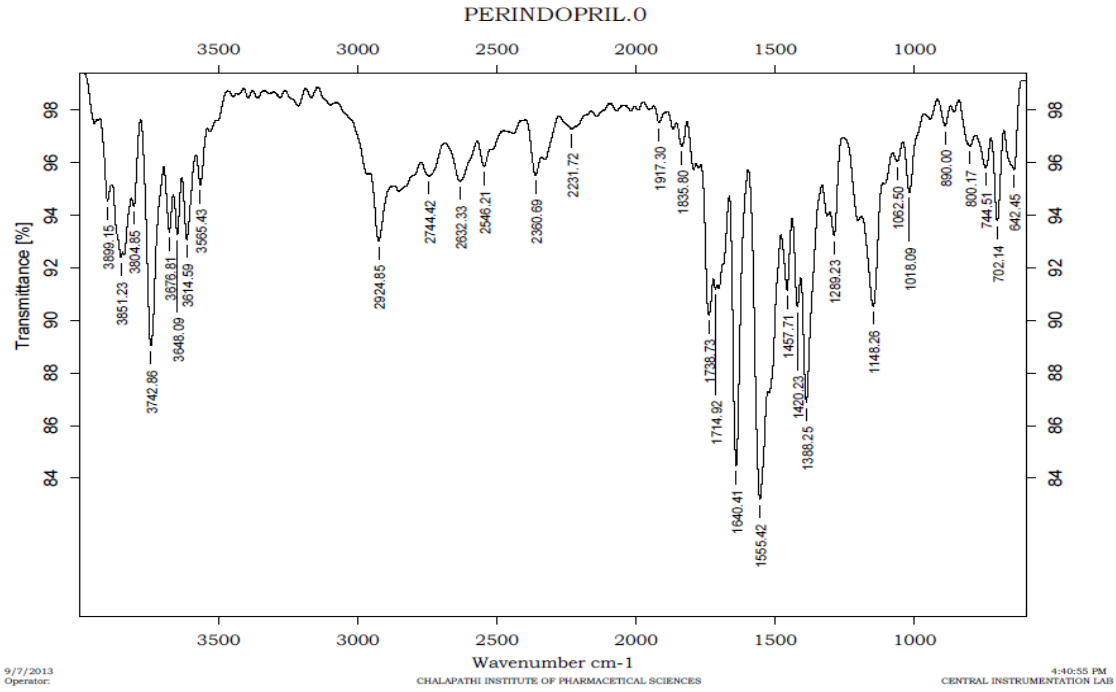
**Dissolution test**

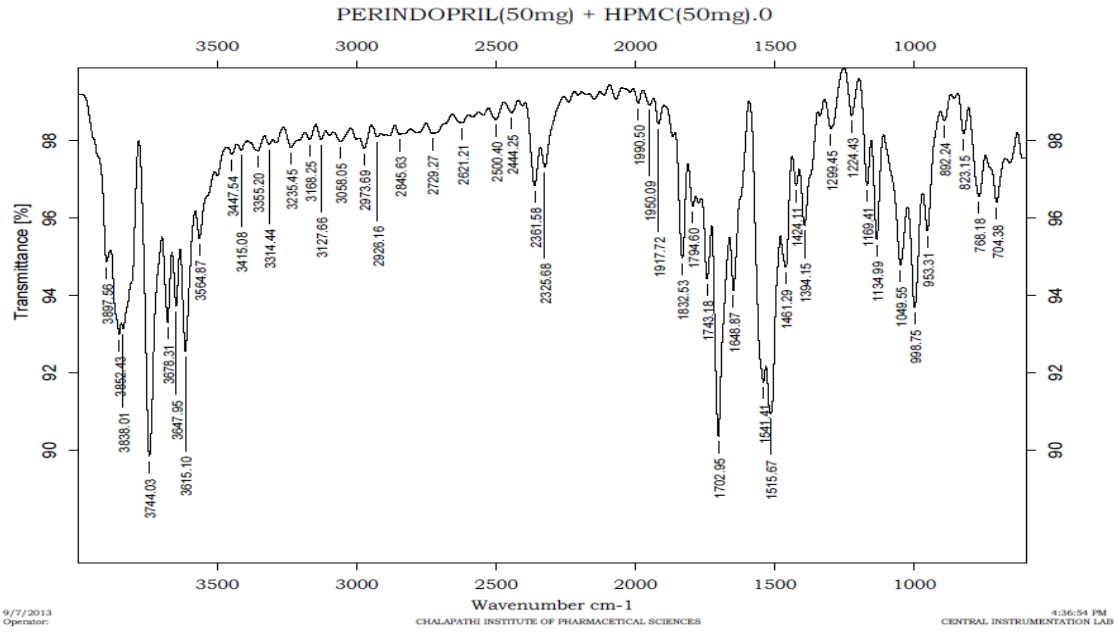
Dissolution testing can be performed using the standard basket or paddle apparatus described in any of the pharmacopoeia. The dissolution medium will essentially be selected as per the sink conditions and highest dose of the API. Many times the dissolution test can be difficult due to tendency of the strip to float onto the dissolution medium when the paddle apparatus is employed.

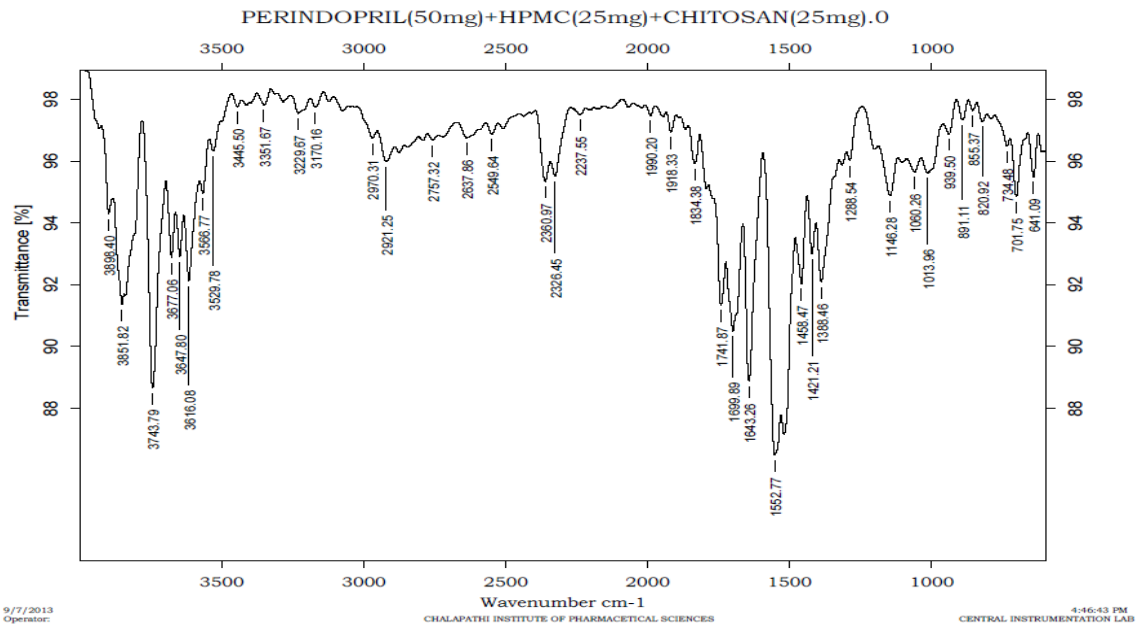
## RESULTS AND DISCUSSION

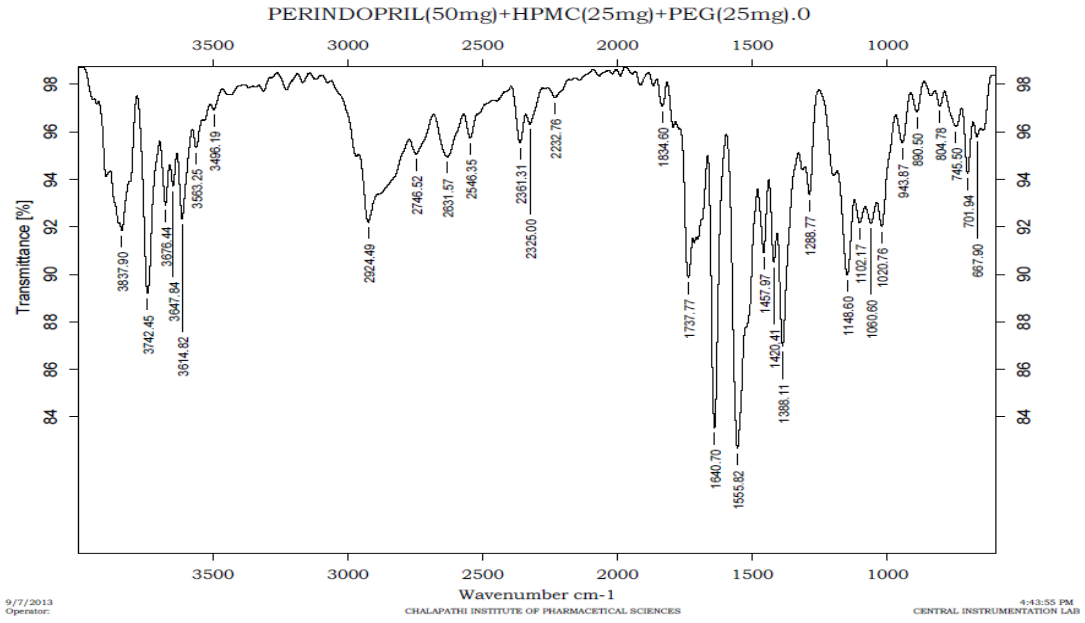
### Preformulation Studies

The pre formulation studies were done by FTIR spectroscopy method. The IR spectra of pure drug and polymers were compared with IR spectra of the powder blend of the various formulations. The absence of appearance or disappearance of characteristic peaks in the spectra confirms that there was no incom patability between the drug and the polymers taken for the study.






**In vitro drug release data for F1 (perindopril 4mg; HPMC 250mg; Chitosan 125mg) (1:0.5)**

| Time in mts | Absorbance | Concentation | Amount dissolved | % Amt dissolved | %Amt un -dissolved | Log% Amnt un-dissolved |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 100 | 2 |
| 5 | 0.00778 | 1.01 | 3.03 | 75.75 | 24.25 | 1.38 |
| 10 | 0.00832 | 1.04 | 3.12 | 78.00 | 22.00 | 1.34 |
| 15 | 0.00922 | 1.09 | 3.27 | 81.75 | 18.25 | 1.26 |
| 30 | 0.00994 | 1.13 | 3.41 | 85.25 | 14.75 | 1.16 |
| 60 | 0.01066 | 1.17 | 3.53 | 88.25 | 11.75 | 1.07 |

**In vitro drug release data for F2 (perindopril 4mg; HPMC 250mg; Chitosan 250mg) (1:1)**

| Time in mts | Absorbance | Concentration | Amont dissolved | % Amt dissolved | %Amt un -dissolved | Log% Amnt un-dissolved |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 100 | 2 |
| 5 | 0.00644 | 0.936 | 2.81 | 70.25 | 29.75 | 1.47 |
| 10 | 0.007474 | 0.993 | 2.98 | 74.50 | 25.50 | 1.40 |
| 15 | 0.008608 | 1.056 | 3.17 | 79.25 | 20.75 | 1.31 |
| 30 | 0.009094 | 1.083 | 3.25 | 81.25 | 18.75 | 1.27 |
| 60 | 0.00994 | 1.13 | 3.39 | 84.75 | 15.25 | 1.18 |

**In vitro drug release data for F3 (perindopril 4mg; HPMC 350mg; Chitosan 175mg) (1:0.5)**

| Time in mnts | Absorbance | Concentration | Amount dissolved | % Amt dissolved | %Amt un -dissolved | Log% Amnt un-dissolved |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 100 | 2 |
| 5 | 0.007114 | 0.973 | 2.92 | 73.00 | 27.00 | 1.43 |
| 10 | 0.007834 | 1.013 | 3.04 | 76.00 | 24.00 | 1.38 |
| 15 | 0.009094 | 1.083 | 3.25 | 81.25 | 18.75 | 1.27 |
| 30 | 0.01012 | 1.140 | 3.42 | 85.50 | 14.50 | 1.16 |
| 60 | 0.01094 | 1.186 | 3.56 | 89.00 | 11.00 | 1.04 |

**In vitro drug release data for F4 (perindopril 4mg; HPMC 350mg; Chitosan 350mg) (1:1)**

| Time in mts | Absorbance | Concentration | Amont dissolved | % Amt dissolved | %Amt un -dissolved | Log% Amnt un-dissolved |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 100 | 2 |
| 5 | 0.0067 | 0.95 | 2.87 | 71.75 | 28.25 | 1.45 |
| 10 | 0.0076 | 1.00 | 3.01 | 75.25 | 24.75 | 1.39 |
| 15 | 0.0085 | 1.05 | 3.15 | 78.75 | 21.25 | 1.32 |
| 30 | 0.00886 | 1.07 | 3.22 | 80.50 | 19.50 | 1.29 |
| 60 | 0.00976 | 1.12 | 3.36 | 84.00 | 16.00 | 1.20 |

**In vitro drug release data for F5 (perindopril 4mg; HPMC 450mg; Chitosan *225mg*) (1:0.5).**

| Time in mts | Absorbance | Concentration | Amont dissolved | % Amt dissolved | %Amt un -dissolved | Log% Amnt un-dissolved |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 100 | 2 |
| 5 | 0.00706 | 0.97 | 2.91 | 72.75 | 27.25 | 1.43 |
| 10 | 0.00778 | 1.01 | 3.03 | 75.75 | 24.25 | 1.38 |
| 15 | 0.00922 | 1.09 | 3.29 | 82.25 | 17.75 | 1.24 |
| 30 | 0.00994 | 1.13 | 0.40 | 85.00 | 15.00 | 1.17 |
| 60 | 0.01066 | 1.17 | 3.52 | 88.00 | 12.00 | 1.07 |

**In vitro drug release data for F6 (perindopril 4mg; HPMC 450mg; Chitosan 450mg) (1:1)**

| Time in mts | Absorbance | Concentration | Amount dissolved | % Amt dissolved | %Amt un -dissolved | Log% Amnt un-dissolved |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 100 | 2 |
| 5 | 0.00688 | 0.96 | 2.90 | 72.5 | 27.5 | 1.43 |
| 10 | 0.0076 | 1.00 | 3.01 | 75.25 | 24.75 | 1.39 |
| 15 | 0.00832 | 1.04 | 3.13 | 78.25 | 21.75 | 1.33 |
| 30 | 0.00904 | 1.08 | 3.25 | 81.25 | 18.75 | 1.27 |
| 60 | 0.00958 | 1.11 | 3.34 | 83.50 | 16.50 | 1.21 |

**In vitro drug release data for F7(perindopril 4mg; HPMC 250mg; PEG125mg) (1:0.5)**

| Time in mnts | Absorbance | Concentration | Amount dissolved | % Amt dissolved | %Amt un -dissolved | Log% Amnt un-dissolved |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 100 | 2 |
| 5 | 0.00832 | 1.04 | 3.125 | 788.12 | 21.88 | 1.34 |
| 10 | 0.00850 | 1.05 | 3.175 | 79.37 | 20.63 | 1.31 |
| 15 | 0.0100 | 1.134 | 3.403 | 85.07 | 14.93 | 1.17 |
| 30 | 0.0111 | 1.195 | 3.586 | 88.96 | 11.04 | 1.04 |
| 60 | 0.0126 | 1.281 | 3.844 | 96.10 | 3.9 | 0.59 |

**In vitro drug release data for F8(perindopril 4mg; HPMC 250mg; PEG250mg) (1:1)**

| Time in mnts | Absorbance | Concentraion | Amount dissolved | % Amt dissolved | %Amt un -dissolved | Log% Amnt un-dissolved |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 100 | 2 |
| 5 | 0.005188 | 0.866 | 2.600 | 65.00 | 35 | 1.54 |
| 10 | 0.005512 | 0.884 | 2.654 | 66.35 | 33.65 | 1.52 |
| 15 | 0.006376 | 0.932 | 2.796 | 69.90 | 30.01 | 1.47 |
| 30 | 0.00670 | 0.950 | 2.851 | 72.27 | 28.73 | 1.45 |
| 60 | 0.00697 | 0.965 | 2.897 | 85.02 | 27.58 | 1.44 |

**In vitro drug release data for F9(perindopril 4mg; HPMC 350mg; PEG175mg) (1:0.5)**

| Time in mnts | Absorbance | Concentration | Amount dissolved | % Amt dissolved | %Amt un -dissolved | Log% Amnt un-dissolved |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 100 | 2 |
| 5 | 0.004396 | 0.822 | 2.466 | 61.65 | 38.35 | 1.58 |
| 10 | 0.00625 | 0.925 | 2.775 | 69.37 | 30.63 | 1.48 |
| 15 | 0.006358 | 0.931 | 2.795 | 69.87 | 30.13 | 1.47 |
| 30 | 0.00643 | 0.935 | 2.806 | 70.15 | 29.85 | 1.47 |
| 60 | 0.00695 | 0.964 | 2.892 | 89.76 | 27.70 | 1.44 |

**In vitro drug release data for F10(perindopril 4mg; HPMC 350mg; PEG350mg) (1:1)**

| Time in mnts | Absorbance | Concentration | Amount dissolved | % Amt dissolved | %Amt un -dissolved | Log% Amnt un-dissolved |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 100 | 2 |
| 5 | 0.00794 | 1.019 | 3.059 | 76.47 | 23.53 | 1.37 |
| 10 | 0.00886 | 1.070 | 3.211 | 80.27 | 19.73 | 1.29 |
| 15 | 0.00925 | 1.092 | 3.277 | 81.92 | 18.08 | 1.25 |
| 30 | 0.01037 | 1.154 | 3.464 | 86.60 | 13.40 | 1.12 |
| 60 | 0.01058 | 1.166 | 3.499 | 87.47 | 12.53 | 1.09 |

**In vitro drug release data for F11(perindopril 4mg; HPMC 450mg; PEG225mg) (1:0.5)**

| Time in mnts | Absorbance | Concentraion | Amount dissolved | % Amt dissolved | %Amt un -dissolved | Log% Amnt un-dissolved |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 100 | 2 |
| 5 | 0.003874 | 0.793 | 2.380 | 59.5 | 40.50 | 1.60 |
| 10 | 0.005602 | 0.889 | 2.669 | 66.72 | 33.28 | 1.52 |
| 15 | 0.008104 | 1.028 | 3.084 | 77.10 | 22.90 | 1.35 |
| 30 | 00.00832 | 1.04 | 3.120 | 78.00 | 22.00 | 1.34 |
| 60 | 0.00868 | 1.06 | 3.185 | 89.05 | 20.38 | 1.30 |

**In vitro drug release data for F12(perindopril 4mg; HPMC 450mg; PEG450mg) (1:1)**

| Time in mnts | Absorbance | Concenration | Amount dissolved | % Amt dissolved | %Amt un -dissolved | Log% Amnt un-dissolved |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 100 | 2 |
| 5 | 0.00868 | 1.06 | 3.191 | 79.77 | 20.23 | 1.30 |
| 10 | 0.00904 | 1.08 | 3.266 | 81.65 | 18.35 | 1.26 |
| 15 | 0.00947 | 1.104 | 3.3125 | 82.81 | 17.19 | 1.23 |
| 30 | 0.01022 | 1.146 | 3.44 | 86.00 | 14.00 | 1.14 |
| 60 | 0.01292 | 1.296 | 3.89 | 90.25 | 2.75 | 0.43 |

**In vitro drug release data for F13(HPMC+DRUG) (250+4mg)**

| Time in mnts | Absorbance | Concentration | Amount dissolved | % Amt dissolved | %Amt un -dissolved | Log% Amnt un-dissolved |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 100 | 2 |
| 5 | 0.0122 | 1.26 | 3.80 | 95.00 | 5.00 | 0.69 |
| 10 | 0.0124 | 1.27 | 3.81 | 95.25 | 4.75 | 0.67 |
| 15 | 0.0128 | 1.29 | 3.87 | 96.75 | 3.25 | 0.51 |
| 30 | 0.0128 | 1.29 | 3.89 | 97.25 | 2.75 | 0.43 |
| 60 | 0.013 | 1.31 | 3.95 | 98.75 | 1.25 | 0.096 |

**In vitro drug release data for F14(HPMC+DRUG) (350+4mg)**

| Time in mnts | Absorbance | Concentration | Amount dissolved | % Amt dissolved | %Amt un -dissolved | Log% Amnt un-dissolved |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 100 | 2 |
| 5 | 0.0106 | 1.17 | 3.52 | 88 | 12.00 | 0.30 |
| 10 | 0.0115 | 1.22 | 3.66 | 91.5 | 8.50 | 0.92 |
| 15 | 0.0121 | 1.25 | 3.77 | 94.25 | 5.75 | 0.75 |
| 30 | 0.01228 | 1.26 | 3.79 | 94.75 | 5.25 | 0.72 |
| 60 | 0.01 | 1.31 | 3.94 | 98.50 | 1.50 | 0.17 |

**In vitro drug release data for F15(HPMC+DRUG) (450+4mg)**

| Time in mnts | Absorbance | Concentration | Amount dissolved | % Amt dissolved | %Amt un -dissolved | Log% Amnt un-dissolved |
|---|---|---|---|---|---|---|
| 0 | 0 | 0 | 0 | 0 | 100 | 2 |
| 5 | 0.0106 | 1.17 | 3.52 | 88 | 12.00 | 0.30 |
| 10 | 0.0115 | 1.22 | 3.66 | 91.5 | 8.50 | 0.92 |
| 15 | 0.0121 | 1.25 | 3.77 | 94.25 | 5.75 | 0.75 |
| 30 | 0.01228 | 1.26 | 3.79 | 94.75 | 5.25 | 0.72 |
| 60 | 0.01 | 1.31 | 3.94 | 98.50 | 1.50 | 0.17 |

**%Drug Content**

| Formulation | %Drug Content |
|---|---|
| F1 | 88.25 |
| F2 | 84.75 |
| F3 | 89.00 |
| F4 | 84.00 |
| F5 | 88.00 |
| F6 | 83.50 |
| F7 | 96.10 |
| F8 | 85.02 |
| F9 | 72.30 |
| F10 | 89.76 |
| F11 | 89.05 |
| F12 | 90.25 |
| F13 | 98.75 |
| F14 | 98.50 |
| F15 | 94.50 |

**Disintegration Time(Sec)**

| Formulation | Time(sec) |
|---|---|
| F1 | 49 |
| F2 | 53 |
| F3 | 51 |
| F4 | 54 |
| F5 | 53 |
| F6 | 59 |
| F7 | 43 |
| F8 | 45 |
| F9 | 49 |
| F10 | 49 |
| F11 | 51 |
| F12 | 53 |
| F13 | 35 |
| F14 | 38 |
| F15 | 41 |

**DISSOLUTION TIME**

| Formulation | Time(sec) |
|---|---|
| F1 | 159 |
| F2 | 169 |
| F3 | 162 |
| F4 | 160 |
| F5 | 163 |
| F6 | 167 |
| F7 | 145 |
| F8 | 147 |
| F9 | 148 |
| F10 | 152 |
| F11 | 156 |
| F12 | 160 |
| F13 | 120 |
| F14 | 127 |
| F15 | 135 |

**Drug Content & Content Uniformity**

| Formulation | Absorbance | %Amt Dissolved |
|---|---|---|
| F1 | 0.00947 | 82.81±1.25 |
| F2 | 0.00904 | 81.65±1.87 |
| F3 | 0.00868 | 79.77±2.34 |
| F4 | 0.00832 | 78.00±2.54 |
| F5 | 0.00868 | 79.62±1.75 |
| F6 | 0.0076 | 75.21±1.89 |
| F7 | 0.0100 | 85.07±1.76 |
| F8 | 0.00697 | 78.42±2.12 |
| F9 | 0.00695 | 81.30±2.65 |

| | | |
|---|---|---|
| F10 | 0.00886 | 80.27±1.35 |
| F11 | 0.00868 | 79.62±2.24 |
| F12 | 0.00947 | 82.81±1.76 |
| F13 | 0.0128 | 96.75±1.42 |
| F14 | 0.0121 | 94.25±1.89 |
| F15 | 0.01048 | 87.47±1.54 |

**Film Thickness**

| Formulation | Thickness(mm) |
|---|---|
| F1 | 0.105±0.001 |
| F2 | 0.109±0.002 |
| F3 | 0.106±0.002 |
| F4 | 0.107±0.001 |
| F5 | 0.105±0.002 |
| F6 | 0.105±0.001 |
| F7 | 0.104±0.001 |
| F8 | 0.101±0.002 |
| F9 | 0.108±0.001 |
| F10 | 0.106±0.002 |
| F11 | 0.103±0.001 |
| F12 | 0.109±0.001 |
| F13 | 0.104±0.002 |
| F14 | 0.105±0.001 |
| F15 | 0.101±0.001 |

**Mean Weight of Formulation (Mg)**

| Formulation | Mean weight(mg) |
|---|---|
| F1 | 36±3.4 |
| F2 | 38±1.2 |
| F3 | 110±7.2 |
| F4 | 104±8.4 |
| F5 | 40±1.0 |
| F6 | 48±2.3 |
| F7 | 77±1.2 |
| F8 | 66±1.4 |
| F9 | 59±1.0 |
| F10 | 104±2.1 |
| F11 | 79±0.9 |
| F12 | 124±4.2 |
| F13 | 45±1.0 |
| F14 | 59±1.0 |
| F15 | 63±2.1 |

**% Moisture Loss**

| Formulation | % Moisture Loss |
|---|---|
| F1 | 0.029 |
| F2 | 0.021 |
| F3 | 0.017 |
| F4 | 0.023 |
| F5 | 0.032 |
| F6 | 0.028 |
| F7 | 0.040 |
| F8 | 0.016 |
| F9 | 0.017 |
| F10 | 0.019 |
| F11 | 0.021 |
| F12 | 0.028 |
| F13 | 0.020 |
| F14 | 0.016 |
| F15 | 0.017 |

**Tensile Strength**

| Formulation | Tensile Strength ($kg/mm^2$) |
|---|---|
| F1 | 1.75±0.23 |
| F2 | 1.73±0.004 |
| F3 | 1.69±0.037 |
| F4 | 1.72±0.091 |
| F5 | 1.71±0.003 |
| F6 | 1.65±0.006 |
| F7 | 1.62±0.040 |
| F8 | 1.58±0.035 |
| F9 | 1.62±0.002 |
| F10 | 1.54±0.15 |
| F11 | 1.61±0.07 |
| F12 | 1.67±0.02 |
| F13 | 1.51±0.042 |
| F14 | 1.56±0.027 |
| F15 | 1.57±0.036 |

**% % Elongation**

| Formulation | %Elongation |
|---|---|
| F1 | 1.125 |
| F2 | 0.930 |
| F3 | 0.935 |
| F4 | 1.10 |
| F5 | 1.125 |
| F6 | 1.150 |
| F7 | 1.150 |
| F8 | 1.175 |
| F9 | 1.187 |
| F10 | 1.196 |
| F11 | 1.225 |
| F12 | 1.175 |
| F13 | 1.225 |
| F14 | 1.203 |
| F15 | 1.150 |

**Surface Ph of Film**

| Formulation | Surface ph of film |
|---|---|
| F1 | 6.4±0.13 |
| F2 | 6.6±0.16 |
| F3 | 6.5±0.18 |
| F4 | 6.4±0.15 |
| F5 | 6.7±0.12 |
| F6 | 6.5±0.14 |
| F7 | 6.8±0.11 |
| F8 | 6.3±0.15 |
| F9 | 6.5±0.13 |
| F10 | 6.7±0.12 |
| F11 | 6.6±0.11 |
| F12 | 6.7±0.15 |
| F13 | 6.3±0.16 |
| F14 | 6.4±0.13 |
| F15 | 6.5±0.18 |

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