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FORMULATION AND CHARACTERIZATION OF BISOPROLOL FAST DISSOLVING FILMS PREPARED BY SOLVENT CASTING METHOD.

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Abstract:

Objective: *This study aims to develop and characterize fast-dissolving films of bisoprolol, a commonly prescribed antihypertensive agent, using the solvent casting method. The objective is to create an oral dosage form that enhances patient compliance through rapid disintegration and drug release.*

Methods: *Bisoprolol fast-dissolving films were formulated using various film-forming polymers and solvents. The solvent casting method was employed to prepare the films, with different polymer ratios and solvent compositions tested to optimize the formulation. The films were characterized for their physical appearance, thickness, tensile strength, and dissolution properties. In vitro drug release studies were conducted to evaluate the disintegration time and release profile of bisoprolol from the films.*

Results: *The films demonstrated uniformity in appearance and a consistent thickness across formulations. The tensile strength varied with polymer composition, indicating that film mechanical properties could be tailored to specific requirements. Dissolution studies revealed that the films disintegrated rapidly, with bisoprolol releasing at an accelerated rate compared to traditional tablet forms. The optimized film formulation achieved a fast disintegration time of less than 30 seconds and a high drug release rate, meeting the criteria for fast-dissolving dosage forms.*

Conclusion: *The solvent casting method successfully produced bisoprolol fast-dissolving films with desirable characteristics, including rapid disintegration and efficient drug release. This formulation offers a viable alternative to conventional oral dosage forms, potentially improving patient adherence and therapeutic outcomes. Future research will focus on long-term stability studies and further optimization to enhance the practical application of these films in clinical settings.*

Keywords: *Bisoprolol, Fast Dissolving Filims*

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INTRODUCTION:

In the late 1970s as an alternative to conventional dosage forms for pediatric and geriatric patients who experience difficulties in swallowing traditional oral solid dosage forms formulate the fast dissolving tablets by using superdisintigrant/s and hydrophilic ingredients which has the higher bioavailability, quick action and most patient compliance. Many FDTs are prepared by using the expensive lyophillisation process and sometimes difficult to carry, store and handle (fragility and friability).also fear of chocking with fast dissolving tablet1 . To eliminate the drawbacks of fast dissolving tablet a fast dissolving film can be placed. Fast dissolving films are very similar to ultra-thin strip of postage stamp in their shape, size and thickness. Fast dissolving films are formulated using polymers, active pharmaceutical ingredients (API), plasticizers, saliva stimulating agents, sweeteners, flavors, preservatives and colors. Fast dissolving film 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. It then rapidly disintegrates and dissolves to release the medication for oromucosal absorption or with formula modifications, will maintain the quick-dissolving aspects allow for gastrointestinal absorption to be achieved when swallowed. Technology Catalysts forecasts the market for drug products in oral thin film formulations to be valued at $500million in 2007 and could reach $2 billion. More importantly, prescriptions of fast dissolving films have been now approved in US, EU and Japan which are the three major regions. These approved Rx films, have potential to dominate over other oral dosage forms of the same drugs. It seems that the value of the overall oral thin film market will grow significantly.

Special features of Fast Dissolving Films:

- Thin elegant film
- Available in various size and shapes
- Unconstructive
- Fast disintegration
- Rapid release
- Have an acceptable taste.
- Give a pleasing mouth feel.
- Should not leave residue in mouth.

Advantages:

- Accessibility of larger surface area that leads to quickly disintegrate and dissolution in the oral cavity within seconds.
- Fast Dissolving Film is flexible so they are not as fragile and need not any kind of special package for protection during transportation and storage as compared to FDT.
- No need of water has led to better satisfactoriness amongst the dysphasic patients.
- No fear of chocking as compared to FDT.
- The large surface area available in the film dosage form allows rapid wet by saliva then quickly disintegrates and dissolve and absorbed directly and can enter the systemic circulation without undergoing first-pass hepatic metabolism and on increase the bioavailability
- The dosage form can be consumed at any place and any time as per convenience of the individual.

Disadvantages:

- Dose uniformity is a technical challenge
- Hygroscopic in nature
- High doses cannot be incorporated
- Require special packaging for products stability and safety.

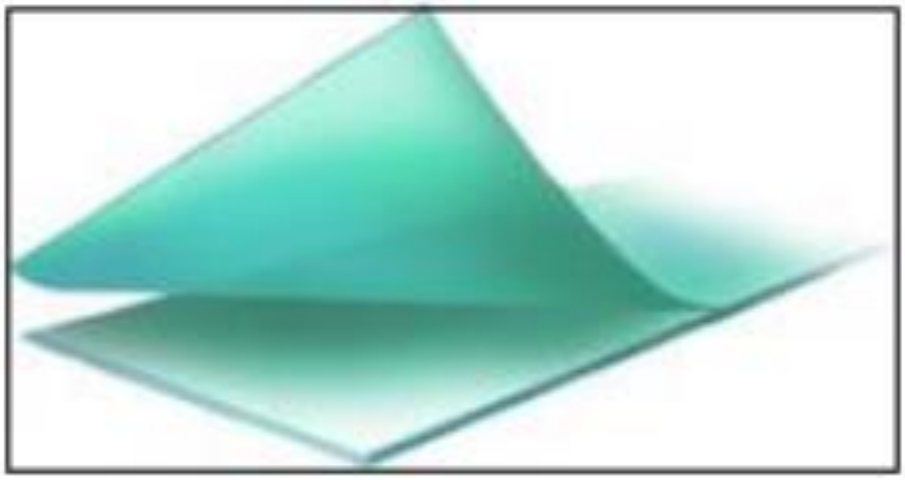

Figure 1.1 : Fast Dissolving Film

Composition of the system:

Fast dissolving film is a thin film with an area of 2-8 cm2 containing an active ingredient. The immediate dissolution, in water or saliva is reached through a special matrix from watersoluble polymers. Drugs can be incorporated up to a single dose of 30mg. Formulation considerations have been reported as important factors affecting mechanical properties of the films. The excipients used in formulation of fast dissolving films are also discussed in detail. From the regulatory perspectives, all excipients used in the formulation should be generally regarded as safe(i.e.GRASlisted)and should be approved for use in oral pharmaceutical dosage forms.[2]

Active pharmaceutical substance can be from any class of pharmaceutically active substances that can be administered orally or through the buccal mucosa. Like antiulcers, antiasthmatics, antitussive, antihistaminic, antiepileptic, expectorants, antianginal etc. For the effective formulation, dose of drug should be in mgs (less than 20 mg/day). Some of the examples of suitable drug molecule that can be incorporated in the FDF.

The ideal characteristics of a drug to be selected:

- The drug should have pleasant taste.
- The drug to be incorporated should have low dose less than 30mg.
- The drugs with smaller and moderate molecular weight are preferable.
- The drug has stability and solubility in water as well as in saliva.
- It should be partially unionized at the pH of oral cavity.
- It should have the ability to permeate oral mucosal tissue.

Water soluble polymers [3]:

Water-soluble polymers are used as film formers. The use of film forming polymers in dissolvable films has attracted considerable attention in medical and nutraceutical application. The water-soluble polymers achieve rapid disintegration, good mouth feel and mechanical properties to the films. The disintegration rate of the polymers is decreased by increasing the molecular weight of polymer film bases. Some of the water soluble polymers used as film former are HPMC E-3 and K-3, Methyl cellulose A-3, A-6 and A-15, Pullulan, carboxmethylcellulosecekol 30, Polyvinylpyrollidone PVP K-90, Pectin, Gelatin, Sodium Alginate, Hdroxypropylcellulose, Polyvinyl alcohol, Maltodextrins and Eudragitrd10.Polymerized rosin is a novel film forming polymer.

Plasticizers:

Formulation considerations (plasticizer, etc.) have been reported as important factors affecting mechanical properties of films. The mechanical properties such as tensile strength and elongation tothe films have also been improved by the addition of plasticizers. Variation in their concentration may affect these properties. The commonly used plasticizers areglycerol, di-butylpthallate, and polyethylene glycolsetc.

Saliva stimulating agent [4]:

The purpose of using saliva stimulating agents is to increase the rate of production of saliva that would aid in the faster disintegration of the rapid dissolving film formulations. Generally acids which are used in the preparation of food can be utilized as salivary stimulants. E.g.Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid. These agents are used alone or in combination between 2 to 6% w/w of weight of the film.

Surfactants:

Surfactants are used as solublising or wetting or dispersing agent so that the film is getting dissolved within seconds and release active agent immediately. Some of the commonly used are sodium lauryl sulfate, benzalkonium chloride, bezthonium chloride, tweens etc. One of the most important surfactant is polaxamer 407 that is used as solubilizing, wetting and dispersing agent.

Sweetening agents [5]:

Sweeteners have become the important part of pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. The classical source of sweetener is sucrose, dextrose, fructose, glucose, liquid glucose and isomaltose. The sweetness of fructose is perceived rapidly in the mouth as compared to sucrose and dextrose. Fructose is sweeter than sorbitol and mannitol and thus used widely as a sweetener. Polyhydric alcohols such as sorbitol, mannitol, and isomalt can be used in combination as they additionally provide good mouth-feel and cooling sensation. Polyhydric alcohols are less carcinogenic and do not have bitter after taste which is a vital aspect in formulating oral preparations. The artificial sweeteners have gained more popularity in pharmaceutical preparations. Saccharin, cyclamate and aspartame are the first generation of the artificial sweeteners followed by acesulfame-K, sucralose, alitame and neotame which fall under the second generation artificial sweeteners. Acesulfame-K and sucralose have more than 200 and 600 time

sweetness. Neotame and alitame have more than 2000 and 8000 time sweetening power as compared to sucrose. Rebiana which is a herbal sweetener, derived from plant Stevia rebaudiana (South American plant) has more than 200 -300 time sweetness.

Flavoring agents [6]:
Flavoring agents can be selected from the synthetic flavor oils, oleo resins, extract derived from various parts of the plants like leaves, fruits and flowers. Flavors can be used alone or in the combination. Any flavor can be added such as essential oils or water soluble extracts of menthol, intense mints such as peppermint, sweetmint, spearmint, wintergreen, cinnamon, clove, sour fruit flavor such as lemon , orange or sweet confectionary flavors such as vanillin, chocolate ,or fruit essence like apple , raspberry, cherry, pineapple. The amount of flavor needed to mask the taste depends on the flavor type and its strength.

Colour:
A full range of colors is available, including FD&C colors, EU Colours, Natural Colours and custom Pantone matched colours.Some saliva stimulating agents may also be added toenhance the disintegration and to get rapid release.Some of these agents are citric acid, tartaric acid, malicacid, ascorbic acid and succinic acid.

MATERIALS AND METHODS:

Bisoprolol-Provided by SURA LABS, Dilsukhnagar, Hyderabad, HPMC-Fisher Scientific, India, HPMC K100-Morepen labs ltd ,Parwanoo(HP), India,HPMC K1500-Praavar Chemtech, Mumbai,Poly propylene glycol (mL)-Millipore system,D.W-Rankem, Citric Acid-Signet Chemical Corporation, Mumbai, Cross Povidone-S.d.fine chem. Ltd, Mumbai, India, Kyron-T314-Purchased from SD Fine- Chem Limited, Mumbai, Mannitol-Purchased from SD Fine- Chem Limited, Mumbai.

METHODOLOGY:

I Drug Polymer Compatibility Studies Using FTIR
II Construction of Calibration Curve
III Preparation of Fast Dissolving Films
IV Evaluation of Fast Dissolving Films formulation

- Thickness
- Weight of films
- Percentage elongation
- Tensile strength
- Folding endurance
- Drug content estimation
- Disintegration test
- In vitro dissolution test

Drug –Polymer compatibility studies by FT-IR:
Drug polymer compatibility studies were performed by FT-IR (Fourier transform infrared spectroscopy). In order to confirm that the entrapment of drug within the polymeric systems involve only the physical process and no interaction between drug and polymer. FTIR absorption Spectra's were shows no significant interaction between drug and polymers.

Selection of the drug:

- ✓ The Bisoprolol which has significantly different pharmacokinetic profiles.
- ✓ Bisoprolol is a drug that breaks up phlegm, used in the treatment of respiratory diseases associated with viscid or excessive mucus. Bisoprolol is often administered as an active ingredient in cough syrup.
- ✓ Bisoprolol was soluble in water and in solvents.
- ✓ Bisoprolol was stable at salivary pH.

Construction of calibration curve for Bisoprolol:
Determination of λmax:
Bisoprolol λmax was determined by spectrophotometer using pH 6.8 buffer medium. First dissolve 10mg of pure drug in 10ml of 6.8 buffer medium. From this 10µg/ml solution was prepared by using pH 6.8 buffer. 10µg/ml solution absorbance was measured at 200-400 nm range by spectrophotometrically using pH 6.8 buffer as reference solution.

Preparation of calibration curve:

1. **Primary stock solution:** Standard calibration curve of Bisoprolol in 6.8 buffer were prepared. First dissolve 10mg of pure drug in 10ml of 6.8 buffers this is primary stock solution.
2. **Second stock solution:** From the above primary stock solution pipette out 1ml of solution and again make up to 10ml this is secondary stock solution. From this secondary stock solution different concentrations of Bisoprolol (10, 20, 30, 40, and 50 µg/ml) in 6.8 buffers were prepared and absorbance of these solutions measured at 242 nm by spectrophotometrically using pH 6.8 buffer as reference solution.

III. Preparation of Fast Dissolving Films

General method of formulation of Fast Dissolving Films:

Following processes are generally used to manufacture the mouth dissolving film.

1. Solvent casting
2. Semisolid casting
3. Hot melt extrusion
4. Solid dispersion extrusion
5. Rolling method

The current preferred manufacturing process for making this film is solvent casting method. In this method water soluble polymer is dissolved in suitable solvent to make homogenous viscous solution. In this other excipients (plasticizer and sweetner) including drug resinate complex were dissolved under stirring. Then the solution is degassed by keeping it in the sonicator. The resulting bubble free solution poured into petriplate and was kept in oven. Dried film is then cut into the desired shape and size for the intended application.

Preparation of blank films using different polymers:

Procedure

- ❖ Accurately weighed quantity of polymer was dissolved in specific quantity of water.
- ❖ The dissolved polymer was made to a uniform dispersion using a homogenizer.
- ❖ During stirring other excipients (plasticizer and sweetner) were added.
- ❖ Then the solution is degassed by keeping it in the Sonicator.
- ❖ The bubble free solution poured into petriplate and was kept in oven.
- ❖ Then the dried films were used to select the best film forming polymers.

Selection of best film forming polymer

The polymer employed should be non-toxic, non-irritant and devoid of leachable impurities. It should have good wetting and spreadability property. The polymer should exhibit sufficient peel, shear and tensile strengths. The polymer should be readily available and should not be very expensive. Film obtained should be tough enough to avoid the damage while handling or during transportation.

Different Polymers Used For Trails

- Hydroxy propyl methyl cellulose
- HPMC K100
- HPMC K1500

Preparation of Fast Dissolving Film

The fast dissolving films of Bisoprololwere prepared by solvent casting technique. The fast dissolving films were prepared using different polymers like Hydroxy propyl methyl cellulose, HPMC K100 and HPMC K1500. Propylene Glycol (PG) was used as plasticizer. The calculated amount of polymer was dispersed in the solvent with continuous stirring using magnetic stirrer and the homogenous solution is formed. Then add 4 ml of plasticizer. Then the sweetner and flavor was added to drug mixed polymeric solution. Then the solution was kept in sonicator for degassing. Then the bubble free solution was casted on to petriplate and was kept in hot air oven. Dried film is then cut into the desired shape and size (1cm x 1cm) for the intended application. By carrying out the trial and error method different quantity of film forming polymers were used for optimizing the formulation.

Formulation of Bisoprolol Fast Fast dissolving films:

Table: Composition of Bisoprolol Fast dissolving films

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Bisoprolol	5	5	5	5	5	5	5	5	5
HPMC	10	20	30	-	-	-	-	--	-
HPMC K100	-	-	-	10	20	30	-	-	-
HPMC K1500	-	-	-	-	-	-	10	20	30
Poly propylene glycol (mL)	2.5	2.5	2.5	5	5	5	7.5	7.5	7.5
D.W	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S

Citric Acid	15	15	15	15	15	15	15	15	15
Cross Povidone	20	30	40	50	-	-	-	-	-
Kyron-T314	-	-	-	-	20	30	40	50	60
Mannitol	10	10	10	10	10	10	10	10	10
Total weight	100	100	100	100	100	100	100	100	100

EVALUATION OF FAST DISSOLVING FILMS:

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 was measured at three different spots of the films and average was taken[1].

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 as given in the equation below

Tensile strength = Load at breakage/ Strip thickness × Strip Width

The instrument was designed such that it had horizontal wooden platform with fixed scale and attachments for two clips that holds patch under test. Out of the two clips one was fixed and other was movable. Weights were hanged to one end of pulley and the other end of pulley was attached with movable clip. The wooden platform was such fitted that it would not dislocate while the test is running. Three strips of patch were cut having 2cm length and 2cm breadth. The thickness and breadth of strips were noted at three sites and average value was taken for calculation. The rate of change of stress was kept constant with the increment of 0.5g per 2minutes. The elongation was observed and the total weights taken were used for calculation. The tensile strength was calculated by using following formula.

Tensile stress = applied force/ cross sectional area =m × g/ b × t

Where, S = tensile stress in 980 dynes/cm2

m = mass in grams

g = acceleration due to gravity (980 dynes/cm2)

b = breadth of strip in centimeters

t = thickness of strip in centimeters

The strain is change resulting in size of strip after the force was applied to its original size. Therefore, the strain can be given as,

Strain (E) = total elongation / original length = $L-L_o/ L_o$

Where, L = length after force was applied

L0 = original length

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.

% Elongation = Increase in length ×100 / Original length

The percent elongation at break was measured by formula given below.

Strain (E) = total elongation / original length × 100

= L-Lo/ Lo × 100

Where, L = length after force was applied,

Lo = 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.

Physical appearance and surface texture of patch

These parameters were checked simply with visual infection of films and by feel or touch.

Weight uniformity of films

Film (size of 1 cm^2) was taken from different areas of film. The weight variation of each film is calculated.

Drug Content uniformity or Assay of film

The films were tested for drug content uniformity by UV Spectrophotometrical method. Films of 1cm x 1cm square size were cut from three different places from the casted films. Each patch was placed in 10 ml volumetric flask and dissolved in 6.8 phosphate buffer. The absorbance of the solution was measured at 242 nm using UV/visible spectrophotometer. The percentage drug content was determined using the

standard graph and the same procedure was repeated for all the formulations.

***In Vitro* Disintegration time**

The *in vitro* disintegration time of fast dissolving films was determined visually in a glass dish of 8 ml 6.8 pH phosphate buffer with swirling action. The disintegration time is the time when a film starts to break or disintegrate. The in vitro disintegration time was calculated for different patches of the same film and average value was taken.

***In Vitro* Dissolution Study**

In vitro dissolution of Bisoprolol Fast dissolving films was studied in paddle type dissolution test apparatus. 900ml of 6.8 phosphate buffer solution was used as dissolution medium. The stirrer was adjusted to rotate at 50 rpm. The temperature of dissolution medium was maintained at 37±0.5ºC throughout the experiment. Samples of dissolution medium (5ml) were withdrawn by means of syringe fitted with pre-filter at known intervals of time and analyzed for drug release by measuring the absorbance at 242 nm. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Percentage drug release was calculated and plotted against time.

RESULT AND DISCUSSION:

Analytical Method Development for Bisoprolol:

Construction of Calibration Curve:

Bisoprolol λ_{max} was determined by spectrophotometer using pH 6.8 buffer medium. First dissolve 10 mg of pure drug in 10 ml of 6.8 buffer medium. From this 10 µg/ml solution was prepared by using 6.8 buffer. 10 µg/ml solution absorbance was scanned at 200 to 400 nm range by spectrophotometrically using 6.8 buffer as reference solution and λ_{max} was observed at 242 nm. A standard graph of pure drug in suitable medium was prepared by plotting the concentration (µg/ml) on X-Axis and absorbance on Y-Axis. An excellent correlation
co-efficient (R^2=0.999) was observed.

Table: Calibration Curve values of Bisoprolol in phosphate buffer pH 6.8 at λ_{max} =242nm

Concentration (µg/ml)	Absorbance λ_{max} =242 nm
0	0
10	0.121
20	0.224
30	0.339
40	0.447
50	0.559

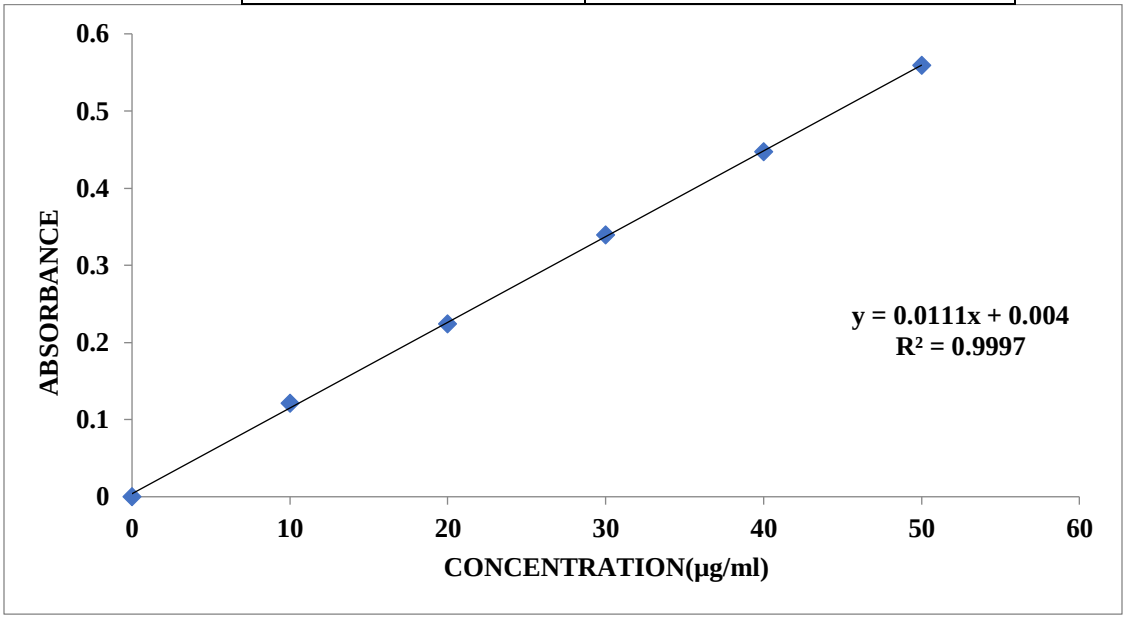

Figure: Calibration curve of Bisoprololin pH 6.8 phosphate buffer at λ_{max} =242 nm

Drug-Excipient Compatibility (FTIR studies):

IR spectral analysis was carried out using FT-IR and the results showed that there were no interactions between drug and Excipients.

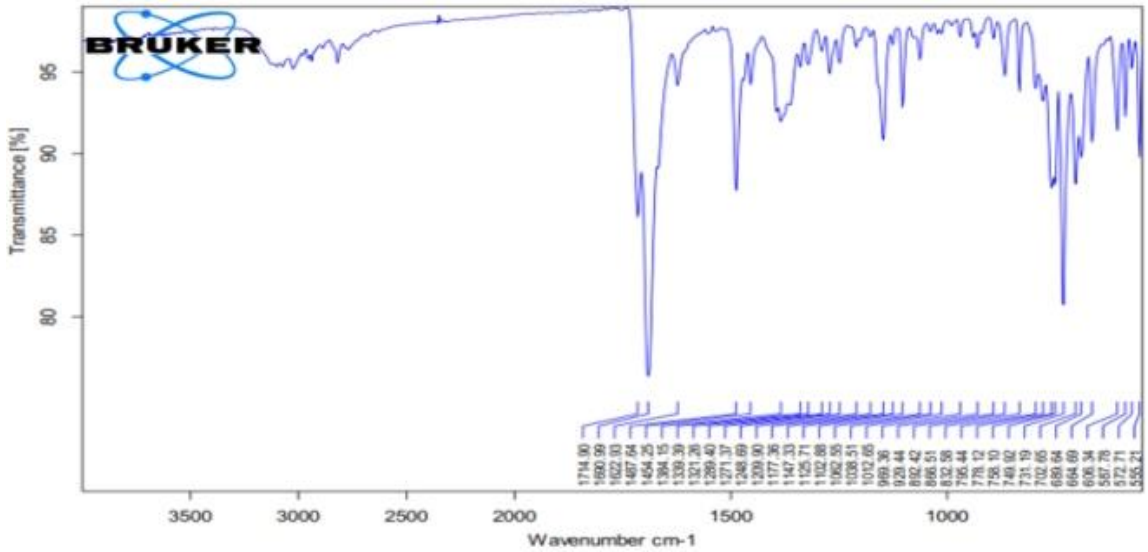

Figure: Bisoprolol Pure Drug FTIR

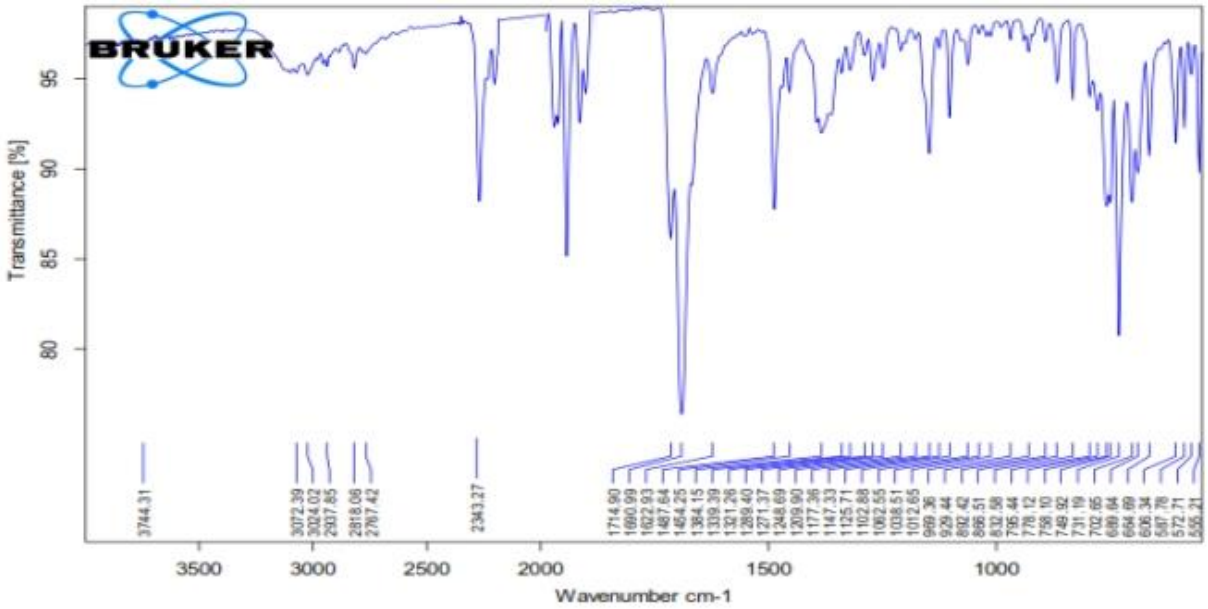

Figure: Bisoprolol Optimized Formulation FTIR

There was no disappearance of any characteristics peak in the FTIR spectrum of drug and the polymers used. This shows that there is no chemical interaction between the drug and the polymers used. The presence of peaks at the expected range confirms that the materials taken for the study are genuine and there were no possible interactions.

Bisoprololis also present in the physical mixture, which indicates that there is no interaction between drug and the polymers, which confirms the stability of the drug.

EVALUATION OF FAST DISSOLVING FILMS:

Fast Dissolving Films were evaluated for the following parameters.

Bisoprolol Fast Dissolving Films were evaluated for

1) Weight Variation
2) Thickness
3) Tensile strength
4) Folding endurance
5) Disintegration time

6) Content uniformity
7) *In Vitro* dissolution studies

Weight Variation

Nine films of Bisoprololeach of 2x2 cm^2 size were cut at five different places from casted films and weight variation was measured. Weight variation varies according to official limits. The results of weight variation are shown in the table.

Thickness: The thickness of the drug loaded films was measured with screwguage. The results of thickness are shown in the table.

Tensile strength& Percent elongation: Tensile strength of the film was determined with digital tensile tester. The film of specific size 3 inch x 10 mm was taken for the test. From the results it is clear that as the concentration of polymer increases the tensile strength of the film also increases. The formulation F4 shows the maximum tensile strength, percent elongation and folding endurance. This might be formation of strong hydrogen bonds between polymer and plasticizer there by imparting flexibility to withstand rupture. The results of Tensile strength & Percent elongation of the film was mentioned in the table.

Folding endurance: Folding endurance was measured manually. A strip of 2 cm^2 was cut and subjected for this study. As the concentration of polymer increases folding endurance of the film also increases. The result of folding endurance of the film was mentioned in the table.

Disintegration Time: Disintegration test was performed in the USP disintegration testing apparatus. Phosphate buffer of pH 6.8 was used as medium. The films were placed in the tubes of the container and the disks were placed over it. Disintegration time of the films was found to be increased with increase in the concentration of the polymer. The results are reported in the table.

Drug Content Uniformity: The prepared formulations were analyzed for drug content and it was observed that all the formulations found to contain almost uniform quantity of drug. The results are reported in the table.

***In- Vitro*-dissolution studies**: Dissolution profiles from films of Bisoprolol were carried out in USP dissolution apparatus-II. The results are reported in the table.

Table: Physical evaluation parameters of all formulations

Formulation Code	Thickness (mm)	Weight Variation (mg)	Disintegration time (sec)	Drug content (%)
F1	2.14	99.12	15	98.32
F2	2.26	98.60	20	99.14
F3	2.28	97.51	18	98.96
F4	2.33	100.05	14	99.61
F5	2.19	98.41	22	99.22
F6	2.19	99.72	19	99.31
F7	2.24	99.14	17	98.07
F8	2.12	97.09	21	98.13
F9	2.25	100.14	19	99.10

Table: Evaluation of transdermal films

Formulation Code	Folding endurance	Flatness (%)	Appearance
F1	61± 2.06	97	Transparent
F2	78± 1.01	96	Transparent
F3	81± 3.19	97	Transparent
F4	85± 2.01	99	Transparent
F5	62± 3.51	95	Transparent
F6	67± 2.28	98	Transparent
F7	75± 2.49	94	Transparent
F8	77± 2.27	93	Transparent
F9	82± 2.61	97	Transparent

Invitro Dissolution Studies:

Invitro dissolution of Bisoprolol Fast Dissolving Films was studied in paddle type dissolution test apparatus. Bowl volume 900 ml of 6.8 phosphate buffer solution was used as dissolution medium. The stirrer was adjusted to rotate at 50 rpm. The temperature of dissolution medium was maintained at 37±0.5ºC throughout the experiment Samples of dissolution medium (5ml) were withdrawn by means of syringe fitted with pre filter at known intervals of time and analyzed for drug release by measuring the absorbance at 242 nm. The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Cumulative percent of Bisoprolol release was calculated and plotted against time.

Table 6-4. *In vitro* drug releases for F1 to F9 formulations

TIME (MINS)	% OF DRUG RELEASE								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	39.31	43.67	48.25	51.22	48.55	44.51	42.51	43.35	41.85
10	47.22	55.34	59.17	64.85	62.91	58.04	49.95	53.17	57.83
15	58.27	73.72	69.78	75.57	67.72	65.68	62.71	66.19	68.41
20	72.18	85.16	81.61	87.25	83.98	76.43	73.13	77.64	79.52
30	88.85	94.75	89.19	99.79	97.31	95.53	87.39	91.06	93.57

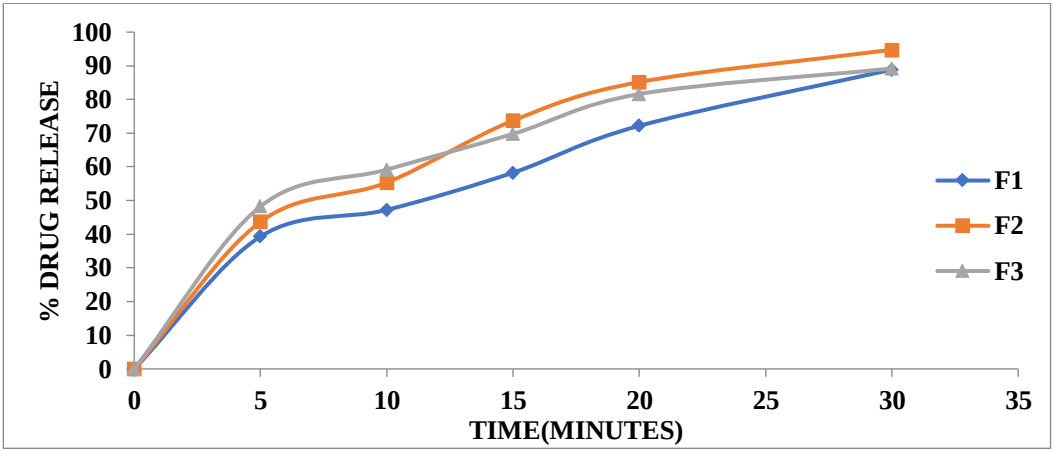

Figure: Comparison curve of *Invitro* drug release for F1- F3 formulations

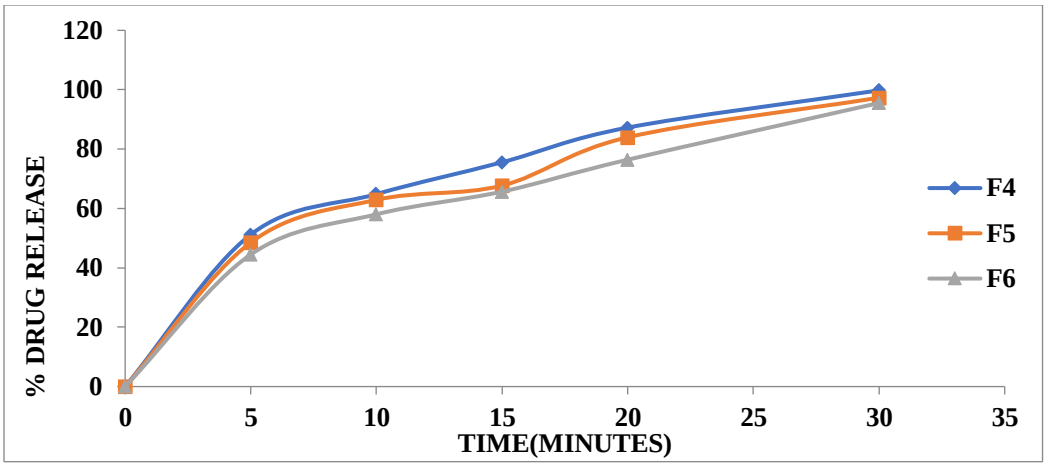

Figure: Comparison curve of *Invitro* drug release for F4- F6 formulations

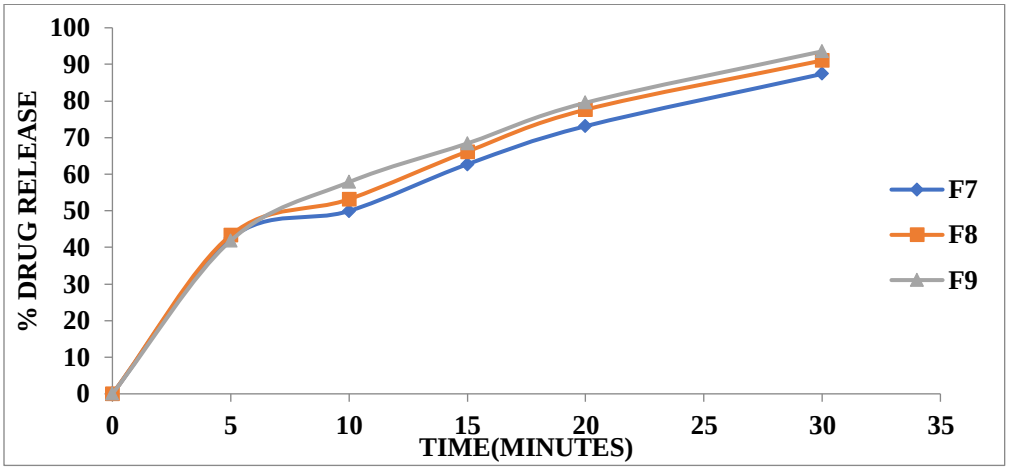

Figure: Comparison curve of *In vitro* drug release for F7- F9 formulations

Invitro dissolution study of formulations F1-F9 shown Good drug release respectively within 30min. Among the all formulations F4 showed good dissolution property. F4 batch contain HPMC K100 as film forming polymer.

DISCUSSION:

Analytical method development for Bisoprolol λ max determination

λ max determination of Bisoprolol pH 6.8 phosphate buffer was determined by using UV Spectrophotometer at 242 nm.

Development of standard graph: Standard plot of Bisoprolol pH 6.8 phosphate buffer were plotted to concentration vs absorbance at 242 nm and the slope value and R^2 value were found to be 0.999.

Evaluation properties: The different Bisoprolol film formulations were evaluated for mechanical properties like thickness, drug content uniformity, folding endurance, tensile strength, weight uniformity, disintegration time, *in vitro* dissolution studies.

Thickness: The thickness of the films from F1-F9 formulations were ranged from 2.33. F4 formulation had the maximum thickness values in all the formulations. From the thickness values it is concluded that as the polymer concentration increases, thickness also increased.

Tensile strength & Percentage elongation : The tensile strength of the films from F1-F9 formulations were ranged from 2.182 to 2.469 kg. F4 formulation had the maximum tensile strength and. From the tensile strength values it is concluded that as the polymer concentration increases, tensile strength and percentage elongation also increased.

Drug content uniformity: The drug content uniformity of the films from F1-F9 formulations were ranged from 97.54 % to 99.61 %. F4 formulation had the maximum drug content uniformity.

Folding endurance: The folding endurance value of the films from F1-F9 formulations were ranged from 52± 3.51 to 75± 2.01. In HPMC K100 containing

formulations as polymer concentration increases folding endurance values were also decreases.

Weight uniformity: Weight uniformity of films was carried out for all the formulations and weight variation varies from 97.09 to 100.14 mg.

Disintegration time: The disintegration time is the time when a film starts to break or disintegrate. The *in vitro* disintegration time was calculated for all the formulations and it ranges from 14 sec to 22 sec Disintegration time of the films was increased with low concentration of the polymer, as more fluid is required to wet the film in the mouth. F4 formulation was quickly disintegrated that is in 14 sec.

Finally selection of the best formulation from all the formulations was carried by using *In Vitro* dissolution studies.

***In vitro* dissolution studies:** *In vitro* dissolution study of F1-F9 formulations were showed different drug release of 94.75 %, 99.79 %, 93.57 %, respectively within 30min. Among the formulations F4 showed good dissolution property hence it is optimized and it contains 10mg of HPMC K100 as film forming polymer.

Small differences were observed in dissolution of drug from the different formulations of the film. Present study reveals that maximum all formulated films showed satisfactory film parameters. Among the optimized formulations F4 formulation showed better drug release of 99.79% within 30 min. F4 formulation contains 10mg of HPMC K100 polymer as film forming agent.

So, it is assumed that 10 mg HPMC K100 containing oral fast dissolving film was optimized in which it showed a drug release of 99.79% compared with other batch formulations.

CONCLUSION:

In this study, we successfully developed and characterized bisoprolol fast-dissolving films using the solvent casting method. The formulation process effectively incorporated bisoprolol into the films, demonstrating promising characteristics in terms of dissolution and mechanical properties. The films exhibited rapid disintegration and high drug release rates, meeting the desired criteria for fast-dissolving oral dosage forms.

The solvent casting method proved to be an efficient technique for producing uniform and consistent films with controlled drug release profiles. Our characterization results, including physical appearance, thickness, tensile strength, and dissolution behavior, confirm that the films are suitable for fast-dissolving applications. The optimized formulation not only enhances the bioavailability of bisoprolol but also offers improved patient compliance due to its ease of administration.

Overall, the bisoprolol fast-dissolving films prepared by the solvent casting method present a viable alternative to conventional oral dosage forms, providing a promising solution for effective and patient-friendly drug delivery. Future studies should focus on further optimizing the formulation parameters and evaluating long-term stability to ensure consistent performance and quality of the films.

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11. Single pouch and Aluminum pouch: Soluble film drug delivery pouch is a peelable pouch for "quick dissolve" soluble films with high barrier properties. The pouch is transparent for product display. Using a 2 structure combination allows for one side to be clear and the other to use a cost-effective foil lamination. The foil lamination has essentially zero transmission of both gas and moisture. The package provides a flexible thin film alternative for nutriceutical and pharmaceutical applications. The single dose pouch provides both product and dosage protection. Aluminum pouch is the most commonly used pouch.
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