



Satankar Rahul *et al*, Int. Journal of Pharmaceutical Sciences and Medicine (IJPSM),
Vol.4 Issue. 8, August- 2019, pg. 13-19

ISSN: 2519-9889

Impact Factor: 3.426

FORMULATION AND EVALUATION OF NITROGLYCERINE ORAL FILM

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ABSTRACT: *The aim of present investigation was to formulate the oral films of Nitroglycerine belongs to a class of drugs known as nitrates. Angina occurs when the heart muscle is not getting enough blood. This drug works by relaxing and widening blood vessels so blood can flow more easily to the heart. Oral films were prepared by solvent casting method using film forming polymers and propylene glycol, PEG 400 as plasticizers and evaluated for mechanical properties, disintegration and in vitro dissolution. All formulations showed good mechanical properties.*

Keywords: - Oral film, Nitroglycerine, Plasticizer, polymer, Solvent casting method.

1. INTRODUCTION

Fast dissolving films for oral administration was a novel approach, for the patients who experience difficulties in swallowing tablets or Capsules. Geriatric, pediatric dysphasic and patients associated with many medical conditions face a problem of difficulty in swallowing the solid formulations. Oral fast-dissolving drug-delivery systems were developed in the late 1970's to overcome the problem of difficulty in swallowing solid formulations. These systems consist of oral film that disintegrate and dissolve quickly in the oral cavity. Oral films and oral strips which rapidly dissolves under the tongue or buccal cavity, could also improve the dissolution of poorly soluble drug. Here we use a drug, Nitroglycerin that is a powerful vasodilator used to prevent chest pain (angina pectoris) by relaxing the smooth muscle of blood vessels in the heart increasing blood flow and oxygen to the heart muscle, and reducing the pumping force the heart must exert to circulate blood through the body. This reduction in the heart's workload relieves the pain of angina pectoris. Nitroglycerin also finds additional utility in controlling blood pressure in preoperative hypertension, or hypertension resulting from intratracheal intubation, anesthesia, skin incision, sternotomy, cardiac bypass, and postsurgical recovery, in addition to producing controlled hypotension during surgery. The oral cavity has been investigated as a site of drug delivery for an extended amount of time. In 1847 Sobrero found that Nitro glycerin was



absorbed from the oral cavity (Ponchel 1993). In Oral film dosage form No water required for administration and No risk of choking. Drug that are unstable in acidic environment like stomach or destroyed in alkaline environment like intestine are often given by this route. The delivery of Drug through the oral tissue layer offers straight forward application, prevents drug degradation by gastrointestinal fluids, avoids First-pass metabolism and probably improves bioavailability with fast drug absorption and quick onset of action.

1.1 Special features of oral films

Thin elegant film, numerous size and shapes, Unconstructive, Wonderful mucoadhesion, Quick disintegration and Fast release of drug.

1.2 Preparation of films

Film formulations were prepared by using following methods:-

Solvent casting method, Hot melts extrusion, semisolid casting method, Solid dispersion and rolling method.

Among all the above methods mentioned, in the present study, solvent casting method was used to formulate Film of Nitroglycerine.

2. MATERIAL & METHODS

Nitroglycerine was purchased from Shirine Corporation Ltd. Indore, HPMC E5, CMC, PEG400 Were procured from SD fine Chemicals, Mumbai. All the Chemicals and reagents were used of analytical and pharmaceutical grade.

3. FORMULATION OF FILM

The different compositions of six films were prepared having same dose of Nitroglycerin. The concentrations of film are mentioned in Table No.1, HPMC-E5 is soaked for overnight in distilled water and stirred for 30 minutes then 5 ml of distilled water was added to PVA and heated up to 80°C. Then the polymeric solutions were mixed thoroughly. Sucrose and citric acid were added to the polymeric solution and stirred for 15 minutes. Drug, tween 80, menthol were dissolved in 5 ml of methanol and sonicated for 30 minutes. Polymeric solution was added to the drug solution and PEG-400 was added, again stirred for 15 minutes. The resulting solution was poured into the petridish and dried in hot air oven at 40°C. After drying film were removed with the help of sharp blade and kept in desiccators for 24 hrs then cut into small sizes. Piece having area of 2×2 cm² these films were subjected for different evaluation parameters.

4. EVALUATION PARAMETER OF FILM

1. Physical appearance

Physical appearance was checked by visual inspection through naked eye.

2. Thickness

Precise film thickness measurements were carried out using screw gauge.

3. Weight variation test

The 4cm² film was cut at three different places in the cast film. The weight of each strip was taken and then the weight variation was observed.



4. Surface pH

The 4cm² film of each formulation was taken and was placed in a Petri dish wetting of the film; the pH at the surface of the film was checked using the pH paper.

5. In-vitro disintegration time

In-vitro disintegration time is determined visually in a petridish of 20 ml distilled water with swirling for every 10 seconds. The disintegration time is the time when the film starts to break or disintegrates.

6. Folding endurance

Folding endurance was determined by repeatedly folding the film (2cm x 2cm) at the same place until it breaks at the place of folding. The number of times the film can be folded at the same place without breaking was the folding endurance value.

7. Drug Content

A film of area 2×2cm² was placed in a volumetric flask containing 50 ml of phosphate buffer of pH-6.8 and kept aside for some time to release the total drug present in the film and the volume was made up to 100 ml with the same buffer. Then the absorbance was measured after suitable dilution at 210 nm against drug devoid polymer blank solution in phosphate buffer of pH-6.8, and the content of Nitroglycerine was calculated using standard graph.

8. In-vitro release study

Determination of dissolution profile of films was carried out in a beaker containing 30 ml phosphate buffer (pH 6.8) at 37 ± 0.50 °C. Whole assembly was then placed on a shaker. Sample aliquot (1.0 ml) was withdrawn at different time intervals and replaced with same fresh media. Samples were filtered and diluted with phosphate buffer (pH 6.8) and analyzed by using UV at 210 nm.

5. RESULTS AND DISCUSSION

1. Average Weight of buccal film

The Average weight of each Formulation (F1 to F6) was tested and results are provided in table No.3. The maximum and minimum average wt. were found to be 61.1 mg and 48.3 mg respectively, weight of formulation F6 shows higher weight due to increased quantity of polymer and plasticizer.

2. Thickness of film

The Thickness of film of each formulation (F1 to F6) was tested and results are provided in Table No.3. The maximum and minimum thicknesses of film were found to be 0.12 mm and 0.08 mm respectively. Thickness of formulation F1 shows lower Thickness due to low quantity of polymer and plasticizer.

3. Folding endurance

The films folding endurance of each formulation (F1 to F6) was tested and results are provided in Table No.3. The maximum and minimum folding endurance were found to be 296 and 235 respectively, increased folding endurance of film F3 shows maximum due to increased quantity of Polymers.

4. Drug content

The Drug content of each formulation (F1 to F6) was tested and results provided in Table No.3. The maximum and minimum drug content were found to be 98.8 and 78.43 respectively, formulation F5 shows higher Drug content due to its Compositions of ingredients.

5. In-vitro Drug release

The In Vitro Drug Release of each formulation (F1 to F6) was tested and results provided in Table No.2. The maximum and minimum drug content were found to be 98.53 % and 7.35 % respectively. The prepared films were found to be uniform, flexible and 98.5% of drug was released from F5 film within 6 minutes which was desirable for fast absorption.

Table 1 Formulation Details of oral Film

S.No.	Formulation Code	Amount of Nitroglycerine	Amount of Polymer	Amount of PEG
1	F 1	0.4 mg	100 mg	25 mg
2	F 2	0.4 mg	150 mg	50 mg
3	F 3	0.4 mg	200 mg	50 mg
4	F 4	0.4 mg	250 mg	100 mg
5	F 5	0.4 mg	250 mg	100 mg
6	F 6	0.4 mg	300 mg	250 mg

Table 2. Percentage Drug Release of various Formulations.

Time in min	Formulations % Drug Release					
	F1	F2	F3	F4	F5	F6
1	7.35%	10.29%	14.71%	8.82%	11.76%	8.8%
2	13.23%	17.65%	23.53%	23.52%	25.0%	32.35%
3	26.47%	30.88%	29.41%	32.35%	33.8%	52.94%
4	35.29%	48.53%	42.65%	42.64%	55.8%	72.05%
5	54.41%	67.65%	57.35%	51.47%	66.17%	80.8%
6	60.29%	79.41%	63.24%	60.29%	98.53%	89.70%
7	77.94%	86.76%	76.47%	72.05%	98.53%	94.11%
8	89.70%	91.18%	85.29%	82.35%	98.53%	97.05%
9	98.53%	94.18%	92.65%	91.17%	98.53%	97.05%
10	98.53%	97.06%	97.06%	94.12%	98.53%	97.05%

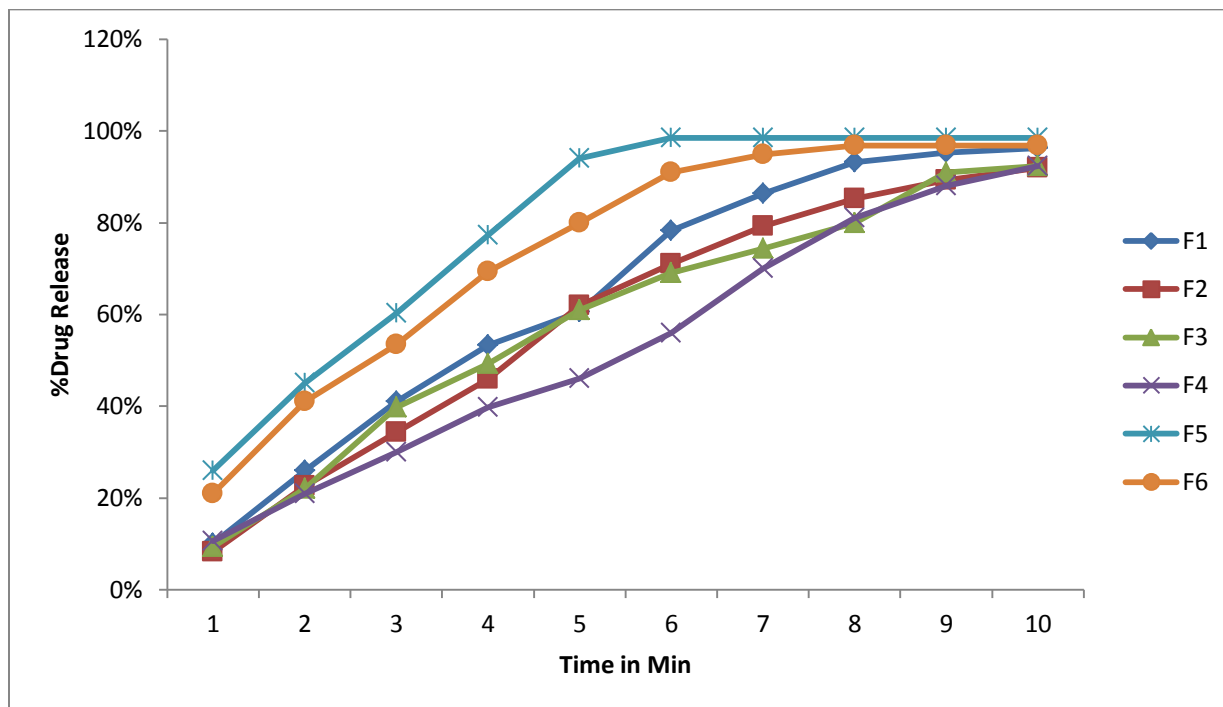


Fig. 1. Comparative study of percentage drug release of film formulations.

Table 3. Evaluation of oral film.

S.No.	Formulation Code	Physical Appearance	Thickness (mm)	Weight (mg)	Surface PH	D.T. (Sec.)	Folding Endurance	Drug Content (%)
1	F 1	Transparent	0.09	48.3	6.6	92	235	78.43
2	F 2	Greasy look	0.10	53.2	6.4	70	248	83.33
3	F 3	Semi-Transparent	0.11	58.4	6.7	70	296	93.13
4	F 4	Semi-Transparent	0.12	49.3	6.5	76	255	83.33
5	F 5	Semi-Transparent	0.14	56.2	6.6	69	252	98.8
6	F 6	Semi-Transparent	0.15	61.1	6.8	90	260	88.24



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6. CONCLUSION

From present investigation it can be concluded that oral fast dissolving films are superior in drug release the films prepared by HPMC E5 and PEG 400 had shown good mechanical strength, drug release, disintegration time and stability. Nitroglycerine administered in the form of fast dissolving films will be potential novel drug dosage form for pediatric, geriatric and also for general population by providing faster release and better patient compliance. Angina is a serious medical condition has become a major public health issue and its prevalence is rapidly increasing among the population. Since it requires immediate pharmacological action, Oral Films becoming an alternative to conventional dosage forms. Among the Six formulations, F5 showing the highest percentage of drug release and shows minimum disintegration time Hence, F5 is considered as the optimized formulation among six Films.

Acknowledgement

The author is thankful to the management of Swami Vivekananda College of pharmacy Indore. For providing necessary facilities to carry out the research work and heartily thankful to my guide Dr. Shikha Agrawal for providing all the support and encouragement to carry out this studies.

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