Available Online through
www.ijpbs.com

International Journal of Pharmacy and Biological Sciences (eISSN: 2230-7605)
IJPBS |Volume 1| Issue 3 |JULY-SEPT |2011|145-159

FORMULATION AND EVALUTION OF RAPIDLY DISSOLVING BUCCAL PATCHES

NARASIMHA RAO R[1], SINDHU REDDY KANDHADI[2], SWAPNA D[3], SUSHMA DEVI KONASREE[4], SWATHI ENUGALA[5]
[1, 2, 3, 4&5] HITS COLLEGE OF PHARMACY, Bogaram (V),Keesara(m)RR.(Dist)-501301
*Corresponding Author Email : rnrao007@yahoo.com

Research Article

RECEIVED ON 16-07-2011 ACCEPTED ON 29-07-2011

ABSTRACT

The objective of the present study was to formulate and evaluate the rapidly dissolving films. The main aim of the work is rapid disintegration and dissolution of the drug Etophylline, which is a bronchodilator used in treatment of asthma. Many pharmaceutical dosage are administered in the form of pills, granules, powers and liquids generally, a pill design is for swallowing intact or chewing to deliver a precise dosage of medication to patients. The pills, which include tablets and capsules, are able to retain their shapes under moderate pressure. However, some patient's particularly pediatric and geriatric patients and also the unconscious patients have difficulty swallowing or chewing solid dosage form. Many pediatric and geriatric patients are unwilling to the take this solid preparations due to fear of choking. In order to assist these patients, several fast-dissolving drug delivery system have been developed Some of the drugs even take a very long time to dissolve, therefore the drug even take much longer time to show its activity, hence our work is aimed to fast dissolution of the drug and maximum bioavailability of bronchodilator Etophylline drug by forming a thin films which are administered orally.

KEYWORDS: Etophylline , Buccal patches , HPMC, Solvent casting method

Introduction

Rapidly dissolving dosage forms are also called quick-dissolving delivery systems; quick-disintegrating, orally disintegrating, mouth dissolve dosage forms; or melt-in-mouth dosage forms. In less than one minute, these dosage forms disintegrate or dissolve in the salivary fluids of the oral cavity, releasing the drug and inactive ingredients. Most of the drug is swallowed with the saliva where subsequent absorption takes place in the gastrointestinal tract. Many pharmaceutical dosages are administered in the form of pills, granules, powders, and liquids. Generally, a pill design is for swallowing intact or chewing to deliver a precise dosage of medication to patients. The pills, which include tablets and capsules, are able to retain their shapes under moderate pressure. However, some patients, particularly pediatric and geriatric patients, have difficulty swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take these solid preparations due to fear of choking[1-9]

In order to assist these patients, several fast-dissolving drug delivery systems have been developed. Fast-dissolving drug delivery was pioneered by scientists at Wyeth Laboratories in the UK during the late 1970s. Even with these differences, most of the existing fast-dissolving drug delivery systems are in the form of solid tablets and designed to dissolve/disintegrate in the patient's mouth within a few seconds or minutes without the need to drink or chew. However, the fear of taking solid tablets and the risk of choking for

certain patient populations still exist despite their short disintegration/dissolution time.

An ideal fast-dissolving delivery system should have the following properties: high stability, transportability, ease of handling and administration, no special packaging material or processing requirements, no water necessary for application and a pleasant taste.

SALIENT FEATURES OF RAPIDLY DISSOLVING DRUG DELIVERY SYSTEM: Ease of administration for patients who are mentally ill, disabled and uncooperative. Requires no water, Quick disintegration and of the dosage form. Overcomes unacceptable taste of the drugs. They Can be designed to leave minimal or no residue in the mouth after administration and also to provide a pleasant mouth feel.Allows high drug loading. Ability to provide advantages of liquid medication in the form of solid preparation. Adaptable and amenable to existing processing and packaging machinery. Cost- effective.

CHARACTERITICS OF FAST DISSOLVING DRUG DELIVERY SYSTEM:

- **Ease of administration:** Fast Dissolving Delivery Systems are easy to administer and handle hence, leads to better patient compliance. Usually, elderly people experience difficulty in swallowing the conventional dosage forms (tablets, capsules, solutions and suspensions) because of tremors of extremities and dysphasia. Fast Dissolving Delivery Systems may offer a solution for these problems

- **Taste of the medicament***:* As most drugs are unpalatable, mouth dissolving delivery systems usually contain the medicament in taste masked form. Delivery systems dissolve or disintegrate in patient's mouth, thus releasing the active ingredients which come in contact with the taste buds and hence, taste masking of the drugs becomes critical to patient compliance.

- **Mouth feel:** Mouth feel is critical, and patients should receive a product that feels pleasant. Any large particles from the disintegrating tablet that are insoluble or slowly soluble in saliva would lead to an unpleasant gritty feeling. This can be overcome by keeping the majority of the particles below the detectable size limit. In some cases, certain flavors can imbibe an improved mouth feel perception, resulting in a product that is perceived as being less gritty, even if the only change is the flavor. Effervescence can be added to aid disintegration and improve mouth feel by reducing the "dryness" of a product

- Hygroscopicity: Several fast dissolving dosage forms are hygroscopic and cannot maintain physical integrity under normal condition from humidity which calls for specialized product packaging[10-16]

COMPOSITION OF THE SYSTEM: Mouth dissolving film is a thin film with an area of 5-20cm^2 containing an active ingredient. The immediate dissolution, in water or saliva respectively, is reached through a special matrix from water-soluble polymers. Drugs can be incorporated up to a single dose of 15mg.formulation considerations (plasticizers etc.) have been reported as important factors affecting mechanical properties of the films, such as shifting the glass transition temperature to lower temperature[17-24]

A typical composition contains the following: Drug -- 1-25%, Water soluble polymer 40-50%, Plasticizers -- 0-20%, Fillers, colours, flavours etc. 0-40%

I. **Drugs:** The different drugs can be used in the formulations like antiulcers (e.g.omeprazole),antiasthamatic

(e.g.etophylline),antitussives, expectorants, etc.

II. **Water soluble polymer:** Water soluble polymers are used as film formers. The use of film forming polymers in dissolvable films as attracted considerable attention in medical and nutraceutical application. The water soluble polymers achieve rapid disintegration, good mouth feel and mechanical properties of the films. The disintegration rate of the polymer is decreased by increasing the molecular weight of polymer film bases. Some of the water soluble polymers used as film former are HPMC , methylcellulose A-3, A-6 and A-15,pullulan ,carboxmethylcellulose cekol-30, polyvinyl pyrolidone, PVP k-90, pectin, Gelatin ,sodium alginate , hydroxyl propyl cellulose, polyvinyl alcohol, Maltdextrins and eudragit 10.

III. **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 to the films have also been improved by the addition of plasticizers. Variation in their concentration may affect these properties. The commonly used plasticizers are glycerol, di-butylpthallate, and polyethylene glycol etc.

IV. **Flavor:** Any flavor can be added, such as intense mints, sour fruit flavors or sweet confectionery flavors.

V. **Color:**A full range of colors is available, including FD&C colors, EU Colors, Natural Colors and custom Pantone-matched colors.

VARIOUS METHODS FOR PREPARATION OF ORAL PATCHES:

One or combination of the following process can be used to manufacture the mouth dissolving films:
i) Solvent casting ii) Semisolid casting iii) hot melt extrusion iv) Solid dispersion extrusion v) Rolling

I. **Solvent casting method:**

In solvent casting method water soluble polymers are dissolved in water and the drug along with other excipients is dissolved in suitable solvent then both the solutions are mixed and stirred and finally casted in to the Petri plate and dried.

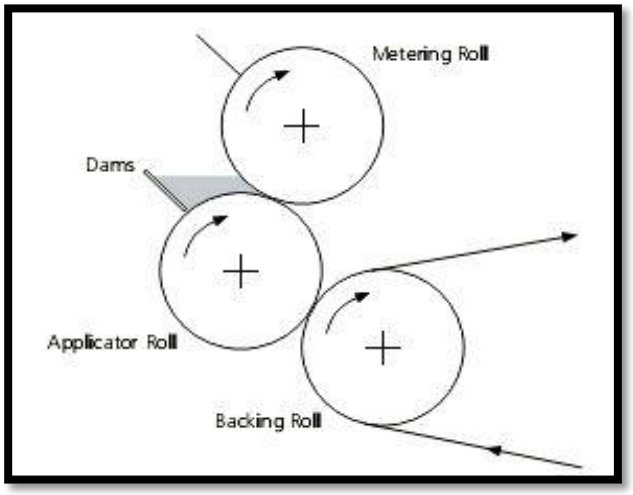
II. **Semisolid casting:** In semisolid casting method firstly a solution of water soluble film forming polymer is prepared. The resulting solution is added to a solution of acid insoluble polymer (e.g. cellulose acetate phthalate, cellulose acetate butyrate), which was prepared in ammonium or sodium hydroxide. Then appropriate amount of plasticizer is added so that a gel mass is obtained. Finally the gel mass is casted in to the films or ribbons using heat controlled drums. The thickness of the film is about 0.015-0.05 inches. The ratio of the acid insoluble polymer to film forming polymer should be 1:4.

III. **Hot melt extrusion:** In hot melt extrusion method firstly the drug is mixed with carriers in solid form. Then the extruder having heaters melts the mixture. Finally the melt is shaped in to films by the dies. There are certain benefits of hot melt extrusion,-Fewer operation units,-Better content uniformity,An anhydrous process.

IV. **Solid dispersion extrusion:** In this method immiscible components are extrude with drug and then solid dispersions are prepared. Finally the solid dispersions are shaped in to films by means of dies.

V. Rolling Method: In rolling method a solution or suspension containing drug is rolled on a carrier. The solvent is mainly water and mixture of water and alcohol. The film is dried on the rollers and cut in to desired shapes and sizes. **Figure No: 1**

Fig No: 1



ADVANTAGES AND DISADVATAGE OF BUCCAL FILMS

The design of thin film are often referred to as PharmFilm, this oral drug delivery technology offers several advantages over other modes of drug delivery, such as ingestible tablets, chewable tablets, orally dissolving tablets, soft gels, liquids or inhalants.The and sublingual and buccal delivery of a drug via thin film has the potential to improve the onset of action, lower the dosing, and enhance the efficacy and safety profile of the medicament.

1. All tablet dosage forms, soft gels and liquid formulations primarily enter the blood stream via the gastrointestinal tract, which subjects the drug to degradation from stomach acid, bile, digestive enzymes and other first-pass effects. As a result, such formulations often require higher doses and generally have a delayed onset of action. Conversely, buccal and sublingual thin-film drug delivery can avoid these issues and yield quicker onsets of action at lower doses.
2. Thin film is more stable, durable and quick dissolving than other conventional dosage forms.
3. Thin film enables to improve dosage accuracy relative to liquid formulations ,since every strip is manufactured in such a way that it contains a precise amount of the drug.
4. Buccal films not only ensures more accurate administration of drug, but also can improve compliance due to the intuitive nature of the dosage form and its inherent ease of administration. These properties are especially beneficial for pediatric, geriatric , unconscious patients and neurodegenerative disease patients where the complete dosage form is different..
5. Buccal films has the ability to dissolve rapidly without the need for water, which provides an alternate way to the patients to swallow and to patients suffering from nausea, such as those patients receiving chemotherapy.

6. Buccal films drug delivery has the potential to allow the development of sensitive drug targets that may not be possible in tablet or liquid formulations.

7. From a commercial perspective thin film drug delivery technology offers an opportunity to extend revenue lifecycles for pharmaceutical companies whose drug patent is expiring and will soon be vulnerable to generic competition.

8. It also avoids the risk and inconveniences of intravenous therapy.

9. Bypass the variation in the absorption and metabolism association with the oral administration.

10. Permits continuous drug administration and the use of drugs with a short biological half-life.

11. Increase the bioavailability and efficacy of the desire of the physician

12. Most of the time lower dose is sufficient.

13. Permits a rapid termination of the medication, if needed ,by simply removing the buccal film from the mouth.

14. patients suffering from dysphasia ,repeated emesis, motion sickness and mental disorders prefers this dosage form as they are unable to swallow large quantity of water.

15. however ,there are some limitations too, the most prominent amongst which is the realization that only a small percentage of the drugs, can be delivered through buccal delivery system.

16. The disadvantage of the most ODT is that they are fragile and brittle ,which warrants special package for protection during storage and transportation. Since the films are flexible they are not as fragile as most of the ODTs .hence ,there is a ease of transportation and during consumer handling and storage.

17. Sublingual film delivers a convenient, quick-dissolving therapeutic dose contained within an abuse-deterrent film matrix that cannot be crushed or injected by patients, and rapidly absorbs under the tongue to ensure compliance.

DRUGS FOR BRONCHIAL ASTHMA

These are the drugs which are used in treatment of asthma. these drugs are classified as:

- **Bronchodilators**:

  1. **B_2 sympathomimetics:** e.g.terbutaline,bambuterol,salmeterol, formoterol, ephedrine.
  2. **Methylxanthines:** e.g. Theophylline, Etophylline,Aminophylline,Hydroxyethyl theophylline, Doxophylline.
  3. **Anticholinergics:** e.g.Ipratropium bromide, Tiotropium bromide.

- **Leukotriene antagonist**:

  e.g. Montelukast, zafirlukast.

- **Mast cell stabilizers**:

  e.g. Sodium cromoglycate, ketotifen.

- **Corticosteroids**:

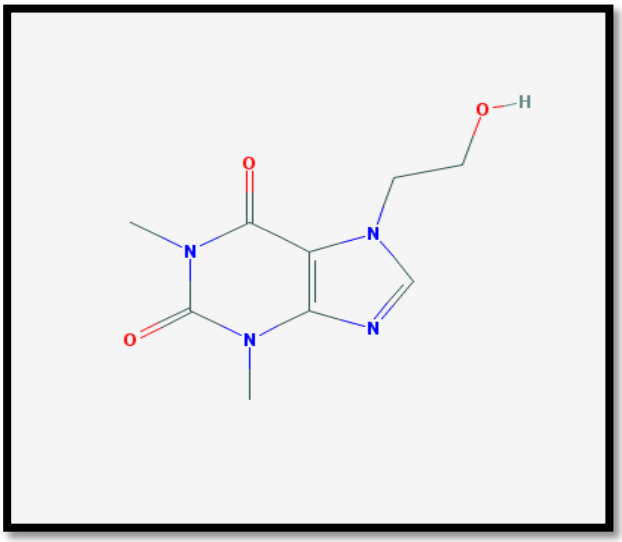
  1.Systemic:

  e.g.Hydrocortisone,prednisolone,

  2.Inhalations:
  e.g.Beclomethasonedipropionate, Budesonide, Fluticasone propionate, Flunisolide, Ciclesonide.

- **Anti-igE antibody**: e.g. omalizumab

DRUG PROFILE :



Chemical name:
7-(2-hydroxyethyl)theophylline.
Synonyms: Cordalin; etofylline Oxphylline; Oxytheonyl;biophylline;Dilaphyllin;Oxyphylline; Frekaphyllin;Sklerodormal;Soluphylline
Molecular weight: 224.22,
Molecular formula: $C_9H_{12}N_4O_3$.,
Melting point: 163^0c.,
Solubility: Water.,
Storage: Solutions may be stored for several days at 4°C.

Mechanism of action:

- It inhibits phosphodiesterase, which degrades cyclic nucleotides, hence increasing the amount of intra cellular CAMP molecules resulting in smooth muscle relaxation.
- Blockage of adenosine receptors (which enhance release of histamine and other inflammatory mediator and bronchospasm).
- **The Overall effect of the drug is to produce:**

Bronchodilation by bronichial muscle relaxation.

1. Suppression of response to the airways to stimuli.
2. Cardiac stimulation (increased heart rate and cardiac output).
3. Respiratory stimulation and it also induces diuresis.

Pharmacokinetics:

It is well absorbed orally, distributed in all tissues, crosses the placenta and is secreted in milk. Upto 60% of the drug binds to the plasma protein . It is mostly metabolized in the liver by demethylation and oxidation. Only 10 % is excreted as unchanged drug, rest of the drug is excreted as changed metabolite in the urine. Steady plasma levels are obtained 1 –3 days after initiation of therapy after which half-life is 6–8 hours. In neonates most of drug is excreted unchanged in urine and clearance is very slow.

MATERIALS AND METHODS: DRUG AND MATERIALS:

Etophylline,HPMC,Menthol,Ethylene glycol,Aspartame, Citric acid were supplied by Chandra labs Hyderabad as a gift sample.

FORMULATION OF ETOPHYYLLINE ORAL PATCHES:

Table No:1 Formulation of buccal patches

S.NO.	INGREDIENTS	FORMULATION-1	FORMULATION-2
1	ETOPHYLLINE	400 mg	400 mg
2	HPMC	500 mg	500 mg
3	MENTHOL	0.072 mg	0.125 mg
4	POLETHYLENE GLYCOL-400	1 ml	1.75 ml
5	ASPARTAME	75 mg	100 mg
6	SUCRALASE	90 mg	90 mg
7	CITRIC ACID	-	10 mg

PREPARATION OF RAPIDLY DISSOLVING FILMS BY USING SOLVNET CASTING METHOD[33-42]: The rapidly dissolving film(RDF)of Etophylline were prepared in lab using polymer HPMC by solvent casting method 400mg of Etophylline was dissolved in 10ml of distilled water containing 500mg of HPMC to which 72-125mg of menthol previously dissolved in 1ml of ethylalcohol(95%) and plasticizer PEG 400 were added sweetener like aspartame (75-112mg) and Sucralase (90-100mg) were also mixed with the above solution .citric acid (0-70mg) and respective flavours(0.1-0.15ml) were also added. The solution was allowed to stand for 30 min. to allow deaeration to take place. The solution was casted on pertidish and dried at room temperature for 24 hours. The film was carefully removed from pertidish, checked for any inperfection and cut into required size to deliver the equivalent dose(2*2cm^2 per strip).The sample were stored in desiccators at relative humidity 30 to 35% until further analysis. The film samples with air bubbles, cut or imperfection were excluded from study. The trials formulation batches are shown in **Table No.1**

EVALUTION OF RAPIDLY DISSOLVING BUCCAL PATCHES: The films were evaluated for the following parameters: [43-52]

Weight variation: Six patches of each formulation were weighed. The weight of each film was noted, by weighing in an electrical balance. Mean weight, standard deviation and percentage coefficient of variation was calculated.

- **Uniformity of film :** The thickness of each film was determined by using a screw gauges at 10 different places of the film. Then mean thickness, standard deviation and percent coefficient of variation was calculated.
- **Area of the film :** The area of the films were determined by using vernier calipers.

- **Density of film :** From the above found weight and thickness, the density of films were calculated by the relationship,

- Density = mass/volume (Volume= area X thickness)

DETERMINATION OF % YIELD OF BUCCAL PATCHES:

After drying, the patches where removed from the Petri dish and were cut into pieces of size 2x2 cm^2. All the films collected were calculated for its % yield by using the formulae:

$$\% \text{ yield} = \frac{\text{Mass of the buccal patches obtained}}{\text{Total weight of the drug and polymer}} \times 100$$

KINETICS OF DRUG RELEASE : it is generally understood that the release of drug from films can be considered as mass transport phenomena involving diffusion of drug molecules from a region of higher concentration to a region of low concentration in the surrounding environment. Attempts to model drug release from release from films have been reported and in the treatment of their data it was assured that the drug release was confined to any of the order such as zero order or first order process. One indication of the mechanism can be obtained using a plot of log cumulative percentage drug remaining in the matrix against time[25-32]

A first order release would be linear as predicted by the following eqution:

$$\text{Log}W_O = Kt/2.303 + \text{log}W$$

Where ,W =amount of the drug left in the matrix ,W_0 = initial amount of the matrix K = first order rate constant ,T = time either in days or hours or minutes. When a log cumulative percentage drug retained v_s time is plotted the curve obtained would be linear indicating first order release. The slope of the curve will be equal to –k/2.303 or k =slope X 2-303.ficks law states that quantity of solute diffusion through a unit cross section of a barrier in unit time(dt) is called as flux(j). J = dq/dt x 1/s.

Flux is proportional to the concentration gradient (dc/dt) in the plane barrier. Therefore when dq x1/s plotted against time(dt) the results curve is linear whose slope is equal to the flux (J). consider a barrier with cross sectional area 's' that separates two compartment be C1 and in the receptor compartment be C2.

Applying fick's law,

J = dq/s.dt(or) dq/dt =Sj (or) J.dt = dq/s

$dq/dt = S.DX (C_1-C_2)/h$

slope of the straight-line passing through origin =J, the flux

(where J= DXdc/dx or $dc/dx=(C_1-C_2)/h$)

The concentration within the barrier is assumed to be constant for a quari-stationary state.C_1-C_2 may be replaced by the partition co-efficient (K) and is given by:

$$K=C_1/Cd=C_2/c_r \text{ (or)}$$

$$K.Cd=C_1 \text{and } Cr=C_2$$

Sink condition provides for the receptor compartment Cr=0

Then dq/dt=D.S.KCd/h(or) dq/dt =P.S.Cd

when D.K/h=P (permeability coefficient), since it is not possible to determine D,K and h independently , it is usually to combine these membrane factor into a single constant P, permeability co-efficient.

Rearranging dq=P.S.Cd.dt for a finite diffusion q=P.S.Cd.dt

P.dt=dq x1/s x Cd

Slope of the straight line passing through origin is equal to 'p', permeability coefficient or

Dq=P.S.Cd.dt rearranging

dq/dt X1/s=P.Cd, therefore dq/dt X1/s=J

J=P.Cd

Hence , P=J/Cd

Where, J=flux ,dq= amount permeated in the receptor sink. dt =time

S=surface area of thin film exposed to medium ,P = permeability coefficient ,Cd = donor concentration.

It is relatively simple to obtain surface area 's' donor concentration Cd ,and the amount of permeate 'q' in the receptor sink,' p' can be obtained from the slope of linear plot of q vs t.

PERCENTAGE MOISTURE LOSS(PML):

Percentage moisture loss was also carried to check the integrity of films at dry condition. Three 2cm diameter films was cut and weighed accurately and kept in desiccators' containing fused anhydrous calcium chloride. After 72 hours the films were removed and weighed. Average percentage moisture loss of three films was found out.

$$\text{Percentage moisture loss} = \frac{\text{Initial weight} - \text{final weight}}{\text{Initial weight}} \times 100$$

INVITRO DISSOLUTION STUDIES: This studies were conducted using 0.1N HCL(900 ml). The dissolution apparatus xxiv at 37+/-0.5^{0}c and at 50 rpm using specified dissolution media. Each film with dimension (2*2 cm^2) was placed on stainless steel wire mesh (700 mm). The film samples was placed on sieve and submerged into dissolution media. Sample containing 10 ml volume were withdrawn at 5, 10, 15, 30,60,75,90,105,120 min time intervals and filtered through 0.45 mm. Whatman filter paper and were analyzed spectrophotometrically at 254 nm.The absorbance value were converted to concentration using standard calibration curve previously obtained by experiment .

FOURIER TRANSFORMED INFRARED SPECTROSCOPY:

The different formulation prepared was scanned for infrared spectroscopy.

For the scanning of the sample the longer wavelength from 500 cm^{-1} to 4000 cm^{-1} was used .

SCANNING ELECTRONE MICROSCOPY(SEM): The formed different samples were cut into size of 2x2 cm^2 and stored to avoid brittleness such formed films were collected and evaluated for SEM analysis .The samples were coated with gold film (of thickness 200nm) and visualized under reduced pressure .Fig No:5

RESULTS AND DISCUSSIONS: Buccal films of Etophylline were prepared by the method of solvent casting method employing square shape of size 2x2cm^2 by using mucoadhesive polymers of HPMC.Ethanol is used as solvent .polyethylene glycol -400 was used as a plasticizer as well as penetration enhancer. The drug delivery system was formulated as a rapidly dissolving buccal drug delivery. The prepared Etophylline buccal films were evaluated or characterized based upon their physic chemical characteristics like PMA ,PML, WVT, thickness, weight variation and drug content and also the evaluation like SEM analysis(**Fig No.5**), DSC analysis(**Fig No.4**), invitro dissolution studies(**Fig No.2&3**), IR analysis were done. The results are shown in **Table No- 2&3** for the invitro drug release by using USP dissolution apparatus(basket

method) was thermo stated at 35+/- 0.5^{0}c.The drug content was determined as described for films. Weight variation and uniformity of drug content were performed according to the IP procedure. Content uniformity was determined by weighing 10 patches individually .

INVITRO DRUG RELEASE STUDIES: The invitro dissolution studies were performed using USP-22 type 1 dissolution apparatus at 50rpm. The dissolution medium consisted of 0.1N hydrochloric acid for 2 hours, maintained at 35^{0}c+/-0.5^{0}c.Analiquot(5ml) was withdrawn at specific time intervals. Drug content was determined by UV –visible spectrophotometry at 254nm.It was made clear that none of the ingredient used in the film formulation interfered with the assay. The release studies were conducted in doublet. **Table No:2&3.**

INVITRO RELEASE PROFILE OF BUCCAL PATCHES (FM-1)

S.no.	Time	Absorbance(ug/ml)	%Drug release
1.	5 min	0.271	34 %
2.	10 min	0.359	44%
3.	15 min	0.438	55%
4.	30 min	0.912	98%
5.	45 min	0.878	95%
6.	60 min	0.642	73%
7.	75 min	0.410	51%
8.	90 min	0.280	32%

Table No.2 Invitro dissolution studies of rapidly dissolving buccal patches of formulation-1

INVITRO DRUG RELEASE PROFILE OF BUCCAL PATCHES(FM-2)

S.no.	Time	absorbance(µg/ml)	%Drug release
1	5 min	0.19	24%
2	10 min	0.268	39%
3	15 min	0.514	51%
4	30 min	0.843	97%
5	45 min	0.713	90%
6	60 min	0.522	53%
7	75 min	0.348	44%
8	90 min	0.23	35%

Table No.3 Invitro dissolution study of rapidly dissolving buccal patches of formulation -2

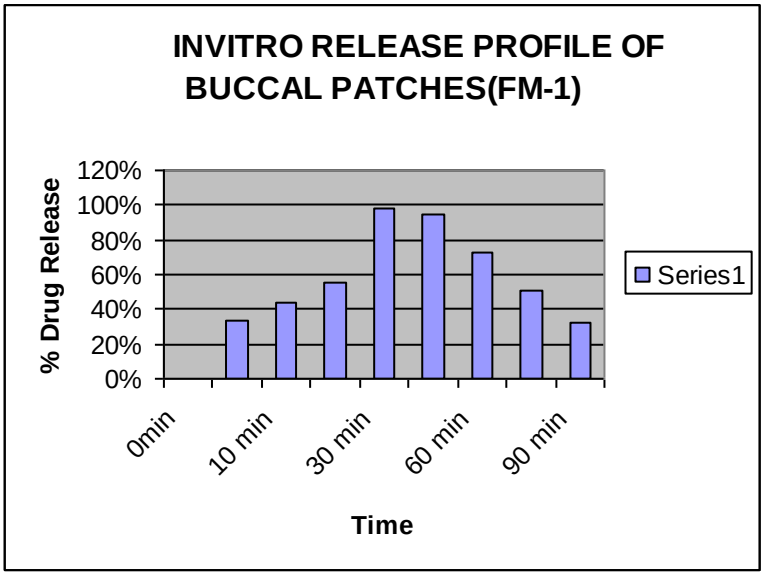


Fig No:2

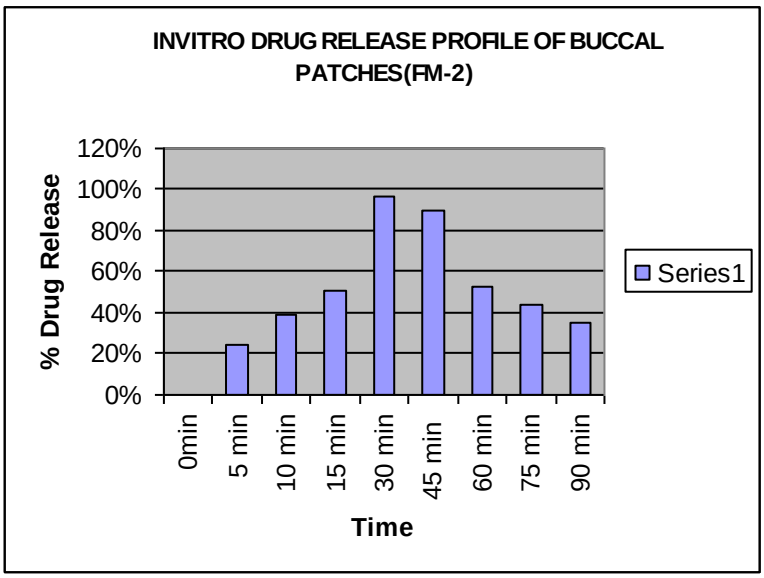


Fig No:3

Module: DSC, Data Name: B140311,Measurement Date: 3/19/2011,Sample Name: P.S. – 1, Sample Weight: 12.914 mg, Reference Name: empty, Reference Weight: 0.000 mg, Comment: from the graph it was found that there was no interaction b/w drug and the polymer Operator: NISHKA Gas1: Nitrogen,Gas2:**Pan: Platinum pan**

Fig. no. 4. shows the DSC graph for the film formulation , which showed that there is no interaction between the drug and the polymer

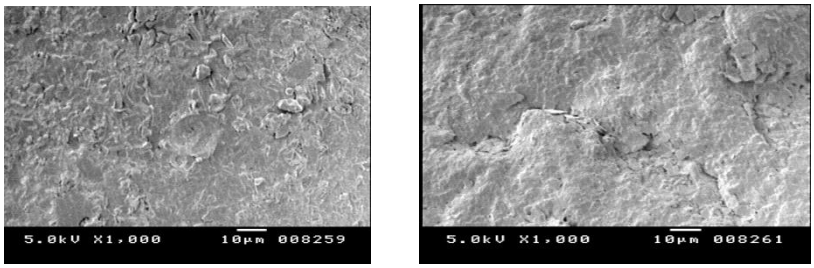


Fig NO.5 SEM Analysis of Formulation-1 and Formulation-2

PERCENTAGE MOISTURE LOSS(PML):

The percentage moisture loss of the buccal patches were performed , primarily the initial weight of the film was found to be 0.2319mg approximately after removed from desiccator the weight was found to be 0.0912mg .From these the percentage loss of moisture was determined. It was found that about 60% of the moisture was losed after removing from the desiccator.

SUMMARY AND CONCLUSION:

Results of the present study demonstrated that the Etophylline drug can be used for the preparation of rapidly dissolving buccal patches .The investigated rapidly dissolving films was capable of dissolving the drug within 30 min and are capable of forming rapid bioavailability of the drug in the plasma .this was expected to increase blood plasma level and reduce the risk of administration. Totally, two formulations were planned and prepared . the characteristics of the films , like weight variation, % moisture loss, % drug yield, drug release studies were evaluated .Invitro dissolution studies were carried out at 50rpm and at a temperature of 35^0c+/-0.5^0c . the data was analyzed as detailed in previous discussion Stability studies at different conditions is also carried out. All the two formulation was found to be thin , rapidly dissolving , transparent. Current literature reveal that , rapidly dissolving buccal patches are gaining their importance and there are many foundation are working on it .this information was encouraging and therefore . this project was taken upto develop Etophylline buccal patches.The patches were also evaluated for the percentage loss of moisture which was found to be about 60%.

REFERENCE

1. proteins. in:D.S.Hsieh (Ed.) , Drug Permeation Enhancement. Theory and Applications, Aungst A, Permeability and metabolism as barriers to transmucosal delivery of peptides and Marcel Dekker, New York, (1994) 323-343.
2. Batchelor H, Novel bioadhesive formulations in drug delivery, The Drug Delivery Companies Report Autumn/Winter, Pharma Ventures Ltd, 2004.
3. Jiménez-Castellanos MR, Zia H, Rhodes CT, Mucoadhe-sive drug delivery systems, Drug Dev. Ind. Pharm. 19 (1993) 143–194.
4. Gohel MC, Sharma R, Soniwala MM. Development of taste masked film of Valdecoxib for oral use.Ind j Pharm Sci. 2007;69:318-320.
5. Jayjock E, Schmitt R, Chein C. Determination of fast dissolve oral film dissolution rate via conductivity.Dow Chemical Company. 2005; 1-4.
6. Joseph R. Robinson, Vincent H. Lee, (1987) " Transdermal Therapeutic Systems" Charpter –12. in " Control drug delivery," 2nd edition Vol (29) ; 523-531pp.
7. Carpel M.C., A.M. Erasmo, S.W. Rowena, P.H. Elizebath, Z. Randoll, (1987), "Drug intellengence and clinical pharmacy" : 642 pp
8. Yie W. Chien "Transdermal drug delivery and delivery systems." Chapter-7 in "Novel drug delivery systems," 2nd edition, Marcel Dekker Inc, Newyork : 302pp
9. Osborne and Hattzenbuler, (1990) " The influence of skin surface lipids on topical formulations," In "Topical drug delivery formulations," David W.

Obsorne, Abntun H. Anamn, Marcel Dekker Inc, 1990 : 70-71 pp.

10. Scheuplein R.J, (1965), "Journal of investigative dermatology" (45) : 335 pp

11. Bell G.H., J.N. Davidson and H. Scarbrough, (1963) Chapter-37, in "Text book of Physiology and Biochemistry," 5th edition, E&S. Lilvingston, Edinburgh .

12. Yie W. Chien, "Transdermal drug delivery and delivery systems", chapter-7 "Novel drug delivery systems", 2nd edition, Marcel Dekkar Inc, New York : 338-344 pp

13. Joseph R. Robinson, Vincent H. Lee, (1987) " Use of Polymers in controlled release of active agent" Chapter-4 in " Controlled drug delivery" 2nd edition Vol. (29) : 180-181 pp.

14. Yie W. Chien, (1987) "Transdermal therapeutic Systems," Chapter-12 in "Controlled drug delivery" 2nd edition, Joseph R. Robinson and Vincent H.Lee, Marcel Dekker, Inc. NY. : 524 pp.

15. Yie W. Chien "Transdermal drug delivery and delivery systems," Chapter-7 in "Novel drug delivery systems," 2nd edition, Marcel Dekker Inc, New York : 361pp.

16. Guy R.H., J. Hadgraft, (1989) " Transdermal drug delivery," Marcel Dekker Inc., N.J., : 59-64 pp.

17. Changs., H.L., (1989) Fund , "Transdermal drug delivery," Guy R.H. and Hadgraft, Marcel Dekker Inc. N.J., :66-77 pp.

18. Rama Rao . P and P.V. Diwan, (1996), " Drug diffusion from Cellulose acetate-PVP free films for tromsdermal administration," "Indian Journal of pharmaceutical science" 58 (6) : 246-250 pp.

19. Chowdary K.P.R., R.A.S. Naidu, April, (1992) "Preparation and evaluation of cellulose acetate films as rate controlling membranes for transdermal use," "Indian drugs" 29(7) : 312-315 pp.

20. Bramhankar D.M., R.M. Karwa, (1996), "Cellulose matrices for controlled release of Keterolac tromethamine," "Indian drugs," 33(3) : 120-123 pp.

21. Tros de llardurya M.C., C. Martin, M.M. Goni and M.C. Martinez oharriz, 1997 " Oxazepam dissolution rate from HPMC Matrices," "Drug Dev. Ind. Pharm," 23(4) : 393-396pp.

22. Narasimha Murthy S. (1997), "Enhancer Synergism of propylene glycol and PEG-400 in Terbutaline Sulphate TDDS," " Indian drugs" 34(4) : 224-226 pp.

23. Rajendran D., G.L. Prabhushankar, S.A. Dhanaraj, Rajeev Dube and B. Suresh, (1996), "Enhance Transdermal delivery of terbutaline sulphate, In-vitro using non-ionic surfactants", " Indian Journal of Pharmaceutical Sciences" : 251-253pp.

24. Michael carbo, Jue-Chen Lin and Lie. W.Chien, (1990), "Bioavailability of propronolol following oral and transdermal administration in rabbits," "Journal of Pharmaceutial Sciences" 76(7) : 584-587 pp.

25. Rooks, Wlt 2d, (1990), "Pharmacotherapy" P.T.Z ; 10(6) : 305-325pp.

26. Dion R. Brocks and Fakhreddin Jamali, (1992), "Clinical Pharmacokinetics of

Keterolac tromethamine," "Clinical Pharmacokinclics" 26(6) : 415-427 pp.

27. Bustamanate, (1993), "General Pharamacol" : 693-398 pp.

28. Domer –F , (1990), "EUR-J-Pharmacol," 177 (3) : 123-135pp.

29. Mutsuo Okumula, Kenjisugibayashi, Keizaburo ogawa and Yasunori morimoto (may, 1989) "Skin permeability of water soluble Drugs," chem-Pharma. Bull 37(5) 1404 – 1406 p

30. Brian L. Strom, Jesse A. Berlin, Judith L. Kinman, Patricia.W, Spiz, Sean Hannessy, Harold feldman, Stephen Kimmel and Jeffrey L. Carson, (1996), Parentral Keterolac and risk of gastro intestinal and operative site bleeding", "JAMA" 25(5) : 36-382 pp.

31. Carolyn J. Rearce, F.M. Gonzalez, J. David Wallin, (1993), "Renal failure and hyperkalemia associated with Keterolac tromethamine", "Archives of internal medicine" 153(4) : 1000-1002 pp.

32. Jonathan P. Purday, Clayton C. Resehert and Pamela Merrick, (1996) "Comparative effects of three doses of intravenous Keterolac tromethamine or morphine and analgesia for relative dental surgery in children", "Canadian Journal of anaesthaetia", 63(3) : 12-1225 pp.

33. Bhalla H.L. and Piyush C. Raj "Release controlling polymers", (Feb 1991), "Indian Drugs" 28(11) : 519 – 522pp.

34. Kanikkannan N, S.B. Jayaswal and J. singh sept 1993 "Transdermal Delivery of Indomethacin : 1. Release profile of drug from polymeric patches", (sept. 1993), "Indian Drugs" 30(9); 441-445 pp.

35. Ramprasad K., N. Udupa, (1995), "Permeation studies of Keterolac" "Pharmag" 17pp

36. Rose Marie Robertson, David Robertson and John A. Oates, (1996) "Analgesic, antipyretic and anti-inflammatory agents and drugs employed in the treatment of gout", Chapter-27 in "The pharmacological basis of therapeutics", 9th edition Joel G. Hasdman, Lee E. Limbard, NY, Mc Graw Hill-health professions division, NY, : 636-637pp.

37. Evart A. Swinyard, Werner Lowenthal, (1985) "Remington's pharmaceutical sciences", 17th edition, Al fanso R. Gennarao, Easton, Mack publishing company, Penmsylvania, :298pp.

38. Susan Budavari, (1989) "The merck index", 11th edition, Merck & Co., Inc., NJ, U.S.A., : 769 pp.

39. Heng P.W.S., L.S.C. Wan, L.F. Wong, (1991) "Effect of HPMC on water penetration in to a penetrating systems", International J. of Pharmaceutics, 73 : 111 pp.

40. USP XXI. The United States Pharmacopoeia, 1219 pp

41. USP XXI. The United States Pharmacopoeia, 2232 pp.

42. Evart A. Swinyard, Werner Lowenthal, (1985) "Remington's pharmaceuticals Sciences", 17th edition, Al fanso R. Gennarao, Easton, Mack Publishing company, penmsylvania, : 1408 pp

43. James A.S., P.M. Shashi and L.Y. James, Theory and practice of Industrial Pharmacy", 3rd edition, LeonLachman, Herbest, Joseph L. Kanig, Bombay, Varghese Publishing house, India : 368-369 pp

44. Susan Budavari, (1989) "The merck index", 11th edition, Merck & Co., Inc., NJ, U.S.A., : 705 pp.

45. Bhalla H.L. and et. al., may, (1991) "Transdermal Films of chlorpheniramine maleate", "Indian Drugs", 28(8) : 369 to 371 pp

46. Susan Budavari, (1989) "The merck index", 11th edition, Merck & Co., Inc., NJ, U.S.A., : 242 pp.

47. Bhatt D.C. and G.P. Agrawal, (1995) "Approach to the Formulation of Promethazine hydrochloride", Eastern Pharmacist, 145-247 pp

48. Udupa N., "Progress in drug delivery research – Manipal experiences". Udupa, Professor, college of pharmaceutical sciences, K.M.C., Manipal, Karnataka. : 140 pp

49. Inderbir Singh, (1990) "Test of significance t-tests", Chapter-4 in "Elementary statistics for medical workers", 1st edition, Jitendar P Vij, Jaypee brothers medical pubishers, (p) limited, EMCA house Ansari Road, New Delhi, : 34-49 pp

50. Ghosh M.N., (1984) "Statistical analysis", Chapter-32 in "Fundamentals of Experimental Pharmacology", 2nd edition, Sinha. J., Scientific book agency, Calcutta, : 179-184 pp

51. Roland Bodmeier and Ornlaksama Paeratakyul (Jan 1990) "Drug release form laminated polymeric films prepared from Aqueous latexes " J. Pharm. Sci., 79(1) : 32-36pp.

52. Lalla J.K., and Y.C. Bageccha, (sept, 1991) "Energetics of Nitroglycerine from monotlithic and membrane controlled systems", Indian Drugs : 28 (12) : 549-562 pp.

*Address for the Correspondence:
NARASIMHA RAO R[1]*
Professor,
[5]HITS COLLEGE OF PHARMACY,
Bogaram (V),Keesara(m)RR.(Dist)-501301
E.mail: rnrao007@yahoo.com