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FORMULATION AND EVALUATION OF ERGOTAMINE TARTARATE BUCCAL FILM

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Abstract:

The objective of present study was to develop matrix type buccal film therapeutic systems of Ergotamine tartrate using various polymers as matrix formers. Ergotamine tartrate buccal films were developed by using solvent casting technique. Various physic mechanical parameters like weight variation, thickness, folding endurance, drug content, moisture content, moisture absorption parameters. An in vitro *drug release study was designed, and it was carried out using buccal film as a membrane. Results revealed that prepared films showed good physical characteristics, no drug-polymer interaction was observed. The in vitro release study revealed that F2 formulation showed maximum release in 8 hrs. The release of Ergotamine tartrate appears to be dependent on polymer of the matrix. Moderately synthetic polymer matrices showed best release. The predominant release mechanism of drug through the fabricated matrices was believed to be by diffusion mechanism. Based upon the in vitro diffusion data the F2 formulation was concluded as optimized formulation.*

Key words: *Buccal film, Buccal drug delivery system, Ergotamine tartrate, synthetic polymers, solvent casting technique, Diffusion mechanism.*

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INTRODUCTION:

The oral route has been seen as a popular and attractive route for the drug administration by many researchers. Reasons for ease of administration, better patient acceptance and compliance, easy preparation of dosage forms and the versatility to administer different type and quantities of drugs. [1] However, there is a number of disadvantages associated with the oral route of drug administration like high first-pass metabolism, ability to cause gastric irritation by drugs, possibilities of degradation of drugs in gastric fluid and delayed onset of action in some cases makes oral mucosal route an important alternative for drug administration [2]. The main feature of the oral mucosal route is to administer the drug into the systemic circulation by diffusing drug through the oral mucosa. [3] The sublingual and buccal mucosa are two routes with the drug can be administered into systemic circulation. Drug administration through these routes and specifically oral mucosal route have many distinctive advantages like circumvention of hepatic metabolism and acid catalyzed degradation in the stomach. [4] The oral mucosal route is the very attractive approach for the systemic administration of macromolecules like proteins and peptides. [5] These macromolecules exhibit superior therapeutic activity compared to other conventional low molecular weight drugs. The avoidance of first-pass hepatic metabolism of drugs when administered via buccal mucosal route can help in improving bioavailability of drugs.[6] Oral drug delivery is a potential alternative to the conventional therapy. The objective of present study was to develop matrix type oral therapeutic systems of Ergotamine tartrate using various synthetic polymers.

MATERIALS:

Ergotamine tartrate was collected as a gift sample from Hetero laboratories, Hyderabad, Polymers and other excipients were purchased from Synpharma Research Labs, HYD

METHODODOLOGY:

Formulation development:

Table-1: Formulation tablae

F.no	Ingredients (mg)					
	Drug (mg)	**Eudragit RS 100 (mg)**	**HPMC k15M (mg)**	**Aspartame(mg)**	**PEG (**ml)	**DMSO** (ml)
F1	2	50	-	2	1	0.1
F2	2	100	-	2	1	0.1
F3	2	-	50	2	1	0.1
F4	2	-	100	2	1	0.1

Preparation of buccal films by solvent casting method:

The solvent casting method is widely used for the preparation of buccal films. A flat bottom glass Petri plate with the diameter of 10 cm was selected for preparing buccal films. A polymeric solution was prepared using solvent solution. To this solution drug solution was added. To this solution, PEG, Aspartame was added. Polymeric solution was mixed under constant stirring for 45 mins. Both permeation enhancers (DMSO) were added to the above solution while mixing. The resulting solution was cast into Petri plate and kept in an oven at 55 °C for 24 hr. [7,8]

FTIR study [9]

FTIR Spectral Studies FTIR spectra of pure drug, polymers and their physical mixtures (stored at 40 ± 2 ^{o}C / 75% ± 5% RH for 2 months) were recorded. The samples were prepared by potassium bromide disc method and scanned for 49 absorbance (Yukinao et al 1997; Mario and Mira 2004; James 2005; John and Wyka 2005).drug and excipients.

Physico- chemical evaluation [10,11,12]:

Physical appearance:

All the formulated Ergotamine tartrate films were observed for color, clarity, flexibility, and smoothness.

Folding endurance:

Buccal films folding endurance was estimated by frequently double over at the same place till it broke.

The number of times the films could be folded at the same place without breaking is the folding endurance. This was restate on all the films for three times and the mean values plus standard deviation was calculated.

Thickness of the films:
The thickness of each films was measured by using screw gauze. Buccal films thickness was estimated at various sites on each film and the average thickness of the buccal film was capture as the thickness of the film.

Weight uniformity:
The formulated buccal films are to be dried at 60^0C for 6 hours before trial. A identify the area of 4.52 cm^2 of films is to be cut in different parts of the film and weigh in digital balance. The average weight and standard deviation values are to be calculated from the individual weights.

Drug content:
The medicated film (2 cm diameter), without backing membrane was allowed to dissolve in 10 mL of simulated saliva solution (pH 6.8) for 2 - 3 h under occasional shaking. The resultant solution was filtered through 0.45 µm filter paper and after suitable dilution, the amount of drug present in the film was determined spectrophotometrically at 275 nm (Shimadzu 1800, Japan).

Swelling behavior
The initial diameter of the original film (2 cm diameter), without backing membrane was determined. Then the sample was allowed to swell on the surface of an agar plate (prepared as described under measurement of surface pH section) kept in an incubator maintained at 37 ± 1 °C. Measurement of the diameter of the swollen film was carried out at predetermined time intervals for 90 min.

Moisture absorption studies:
The buccal films were weighed exactly and placed in a desiccator containing aluminium chloride to maintain 79.50% RH. After 3 days, the films were taken out and weighed. The percentage of moisture uptake was calculated using the following formula.

$$\text{Perentage moisture uptake} = \frac{\text{Final weight} - \text{Initial weight}}{\text{Initial weight}} \times 100$$

Moisture loss studies:
Three films were weighed separately and kept in a desiccator contains calcium chloride at 37^0C for 24 hours. Then the last weight was noted when there was no further change in the weight of the film. The percentage of moisture loss was calculated using the following formula.

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

***In vitro* release study:**
The release rate of the drug was determined by using Franz diffusion cell apparatus temperature maintained at 37 ± 0.5 ^{0}C and stirred at a rate of 200 rpm. Sink conditions was maintained all over the study. The vessel containing 10ml of phosphate buffer pH 6.8 phosphate buffer solution. Aliquots of 1ml of samples were withdrawn at various time meanwhile and then analyzed using a UV Spectrophotometer.

% release rate of drug was determined using the following formula.

$$\text{Perentage drug release} = \frac{Da}{Dt} \times 100$$

Stability studies:
Selected films were subjected to accelerated stability testing by wrapping them in aluminium foil and packing them in glass vials. These films were kept in an incubator maintained at 37 ± 0.5 oC and 75 ± 5% RH for 6 months. The film was stable only up to 37 °C while conducting the stability studies. When the films were kept at 40 °C, the films become pliable and showed instability. Changes in the appearance, residence time, in vitro drug release and drug content of the stored films were investigated after 3 months. The data presented were the mean of three determinations. [13]

RESULTS AND DISCUSSION:

Compatibility studies of drug and polymers:
All these peaks have appeared in formulation and physical mixture, indicating no chemical interaction between Ergotamine tartrate and polymer. It also confirmed that the stability of drug during encapsulation process.

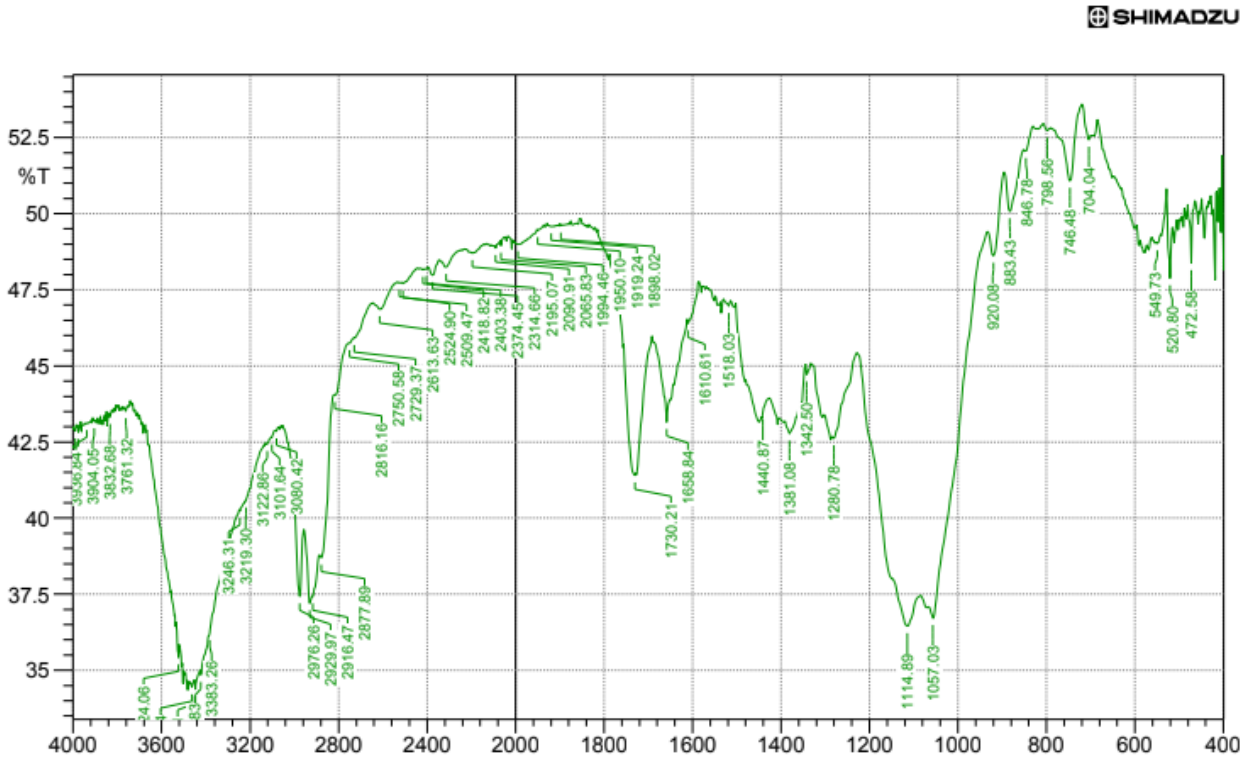

Fig-1: FT-IR Sample for Ergotamine tartrate

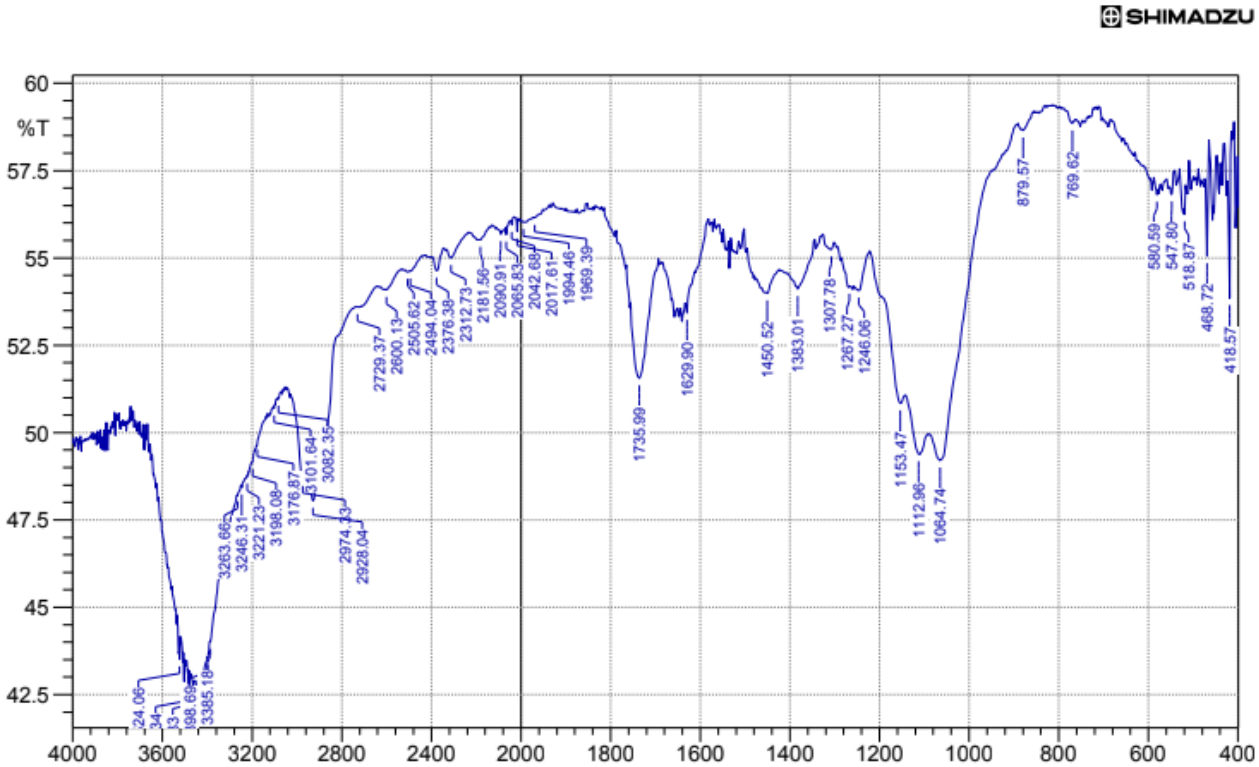

Fig-2: FT-IR Sample for physical mixture of drug and excipients

Physical appearance and surface texture of buccal films:
These parameters were checked simply with visual inspection of films and by feel or touch. The observation reveals that the films are having smooth surface and they are elegant in appearance.

Weight uniformity of buccal films:
The weight of the films was determined using digital balance and the average weight of all films

Thickness of buccal films:
The thickness of the films was measured using screw gauge and the average thickness of all films.

Folding endurance of buccal films:
The folding endurance gives the idea of flexible nature of films. The folding endurance was measured manually, films were folded repeatedly till it broke, and it was considered as the end point. The folding endurance was found optimum and the films exhibited good physical and mechanical properties and the average folding endurance of all films.

Drug content uniformity of buccal films:
Ergotamine tartrate buccal films prepared with various polymers were subjected to the valuation for uniform dispersion of drug throughout the patch. In each case three films were used and the average drug content was calculated.

% Moisture loss:
The moisture content in the buccal films ranged from 8.05 to 8.29 %. The moisture content in the formulations was found to be increased by increase in the concentration of polymers.

% Moisture absorption:
The moisture absorption in the buccal films ranged from 9.06 to 9.18 %.

Swelling index:
The swelling index in the buccal films ranged from 12.56 to 14.10 %.

Table -2: Physicochemical evaluation data of Ergotamine tartrate Buccal Films

F. code	F1	F2	F3	F4
Thickness (mm)	0.39	0.41	0.36	0.42
Weight variation (mg)	42.51	40.28	39.67	35.19
Drug content Uniformity	86.39	89.50	83.21	85.39
Folding endurance	50	43	55	49
% Moisture loss	8.16	8.24	8.29	8.05
% Moisture absorption	9.15	9.06	9.23	9.18
Swelling index	12.56	13.87	12.90	14.10

Drug release studies

Table-3: *In vitro* release data of film F_1 to F_4

Time (hrs.)	F_1	F_2	F_3	F_4
0	0	0	0	0
1	23.72	25.18	26.36	28.98
2	35.42	37.82	37.89	35.16
3	43.56	44.25	41.29	43.25
4	53.56	52.95	54.59	50.92
5	60.16	64.5	62.49	61.25
6	70.42	75.53	79.86	74.88
7	81.93	86.91	82.63	85.52
8	93.52	96.86	94.28	94.69

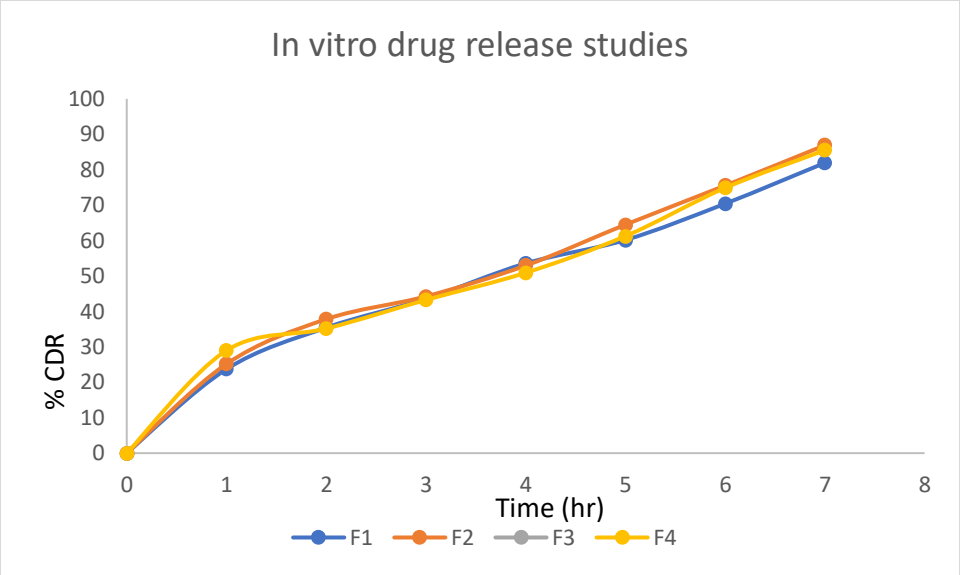

Fig-3: In vitro drug release of (F1- F4) formulation

Stability studies:

Optimized formulations F2 was selected for accelerated stability studies as per ICH guidelines. The films were observed for color, appearance and flexibility for a period of three months. % cumulative drug release of the formulation was found to be decreasing. This decrease may be attributed to the harsh environment (40^0C) maintained during the studies.

Table-4: Stability studies of optimized formulations

S.NO	Time in days	Physical changes	Mean % drug release		
			Ergotamine tartrate		
			25^0C/60%	30^0C/75%	40^0C/75%
1	01	No Change	96.89	96.89	96.89
2	30	No Change	95.82	95.63	95.76
3.	60	No Change	94.12	94.10	94.05
4.	90	No Change	93.26	93.20	93.25

CONCLUSION:

From this study it was concluded that the buccal films containing Ergotamine tartrate can be successfully prepared by using release rate controlling polymers. Hence these formulations of Ergotamine tartrate buccal films with having good permeability.

In the present study it can be concluded that,

- FTIR studies revealed that there is no incompatibility or interaction between Ergotamine tartrate and excipients.
- Formulated buccal films gives satisfactory film characteristics like physical appearance, surface texture, weight uniformity, thickness uniformity, folding endurance, surface pH, percentage moisture uptake, drug content uniformity, in-vitro drug release. The low values for standard deviation for average weight, thickness, surface pH, percentage swelling index, percentage moisture uptake, in vitro drug release and drug content indicated uniformity within the batches.
- Based on in vitro drug release, formulation F2 exhibited a drug release of 96.86 % in 8 hours. The drug release could be retarded more than 8 hr with controlled release behaviour. The prepared buccal films were found to stable after performing stability testing for three month.

- Short term stability studies of optimized formulation as per ICH guidelines indicated that there is no significant changes.

So finally it can be concluded that buccal films of Ergotamine tartrate could provide sustained buccal delivery for prolonged period. A further clinical investigation has to be conducted to establish the safety and efficacy of the developed formulation.

REFERENCES:

1. Sudhakar Y, Knotsu K, Bandopadhyay AK. Bio adhesive drug delivery – A promising option for orally less efficient drugs. J Control Rel 2006;114:15-40.
2. 16. Rajashree Mashru, Vijay Sutariya, Mayur Sankalia, Jolly Sankalia. Transbuccal delivery of lamotrigine across procine buccal mucosa in vitro determination of routes of buccal transport. J Pharm Pharmaceut Sci 2005;8:54-62.
3. Ceschel GC, Maffei P, Moretti MD, Demontis LS, Peana A. International Journal of Pharmaceutics 2000;195:45.
4. Haas J, Lehr CM. Developments in the area of bioadhesive drug delivery systems. Expert Opin Biol Ther 2002;2:287-298.
5. DeVries M.E, Ph.D. Thesis, University of Leiden, Leiden, The Netherlands, 1991.
6. Dixit R.P., Puthli S. P. , Oral strip technology: Overview and future potential, Journal of Controlled Release,2009, 139, 94–107.
7. Rossi Silvia, Sandri Giuseppina, Caramella Carla M., Buccal drug delivery: A challenge already won?, Drug Discovery Today: Technologies, 2005, 2(1).
8. Smart, J.D., The role of water movement and polymer hydration in mucoadhesion. In Bioadhesive drug delivery systems (Mathiowitz, E., Chickering, III D.E.,Lehr, C.M., eds), Marcel Dekker, 1999, PP11–23.
9. Nazilasalamat M, Montakarn C, Thomas J. The use of mucoadhesive polymers in buccal drug delivery. AdvDrug Del Rev 2005;57:1666-91.
10. Gandhi RB, Robinson JR. Oral cavity as a site for bioadhesive drug delivery. Adv Drug Del Rev 1994;13:43-74.
11. Amir HS. Buccal mucosa as a route for systemic drug delivery: A review. J Pharm Pharmceut Sci 1998;1(1):15-30.
12. Salamat-Miller N, Chittchang M, Johnston TP, The use of mucoadhesive polymers in buccal drug delivery, Advance DrugDelivery Review, Nov 2005; 57(11): 1666-1691 .
13. Peppas NA, Buri PA. Surface, interfacial and molecular aspects of polymer bioadhesion on soft tissues. J ContrRel1985;2:257–75.