A REVIEW ARTICLE ON FORMULATION AND EVALUATION OF MUCOADHESIVE BUCCAL PATCHES OF ETORICOXIB

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ABSTRACT

Compared to conventional nonsteroidal anti-inflammatory medications, etoricoxib is a selective cyclooxygenase-2 inhibitor with a lower risk of gastrointestinal effects (NSAIDs). In order to treat chronic pain brought on by osteoarthritis in very elderly individuals as well as an adult group, we assessed the effectiveness and tolerability of etoricoxib. The primary goal of this study is to develop mucoadhesive buccal patches to improve bioavailability, lessen drawbacks like choking while swallowing, especially in the case of tablets and capsules, and prevent the need for water when taking tablets or capsules. Oral films are thin, mucoadhesive polymeric films that can be single or multilayered. Future applications for mucoadhesive buccal patches in the pharmaceutical and nutraceutical industries are enormous. Various active pharmacological substances, film-forming polymers, and other components are used to create the oral films.

Keywords: *Etoricoxib, buccal patches, mucoadhesive, paimkiller*

INTRODUCTION

.1.Transmucosal route of drug delivery.

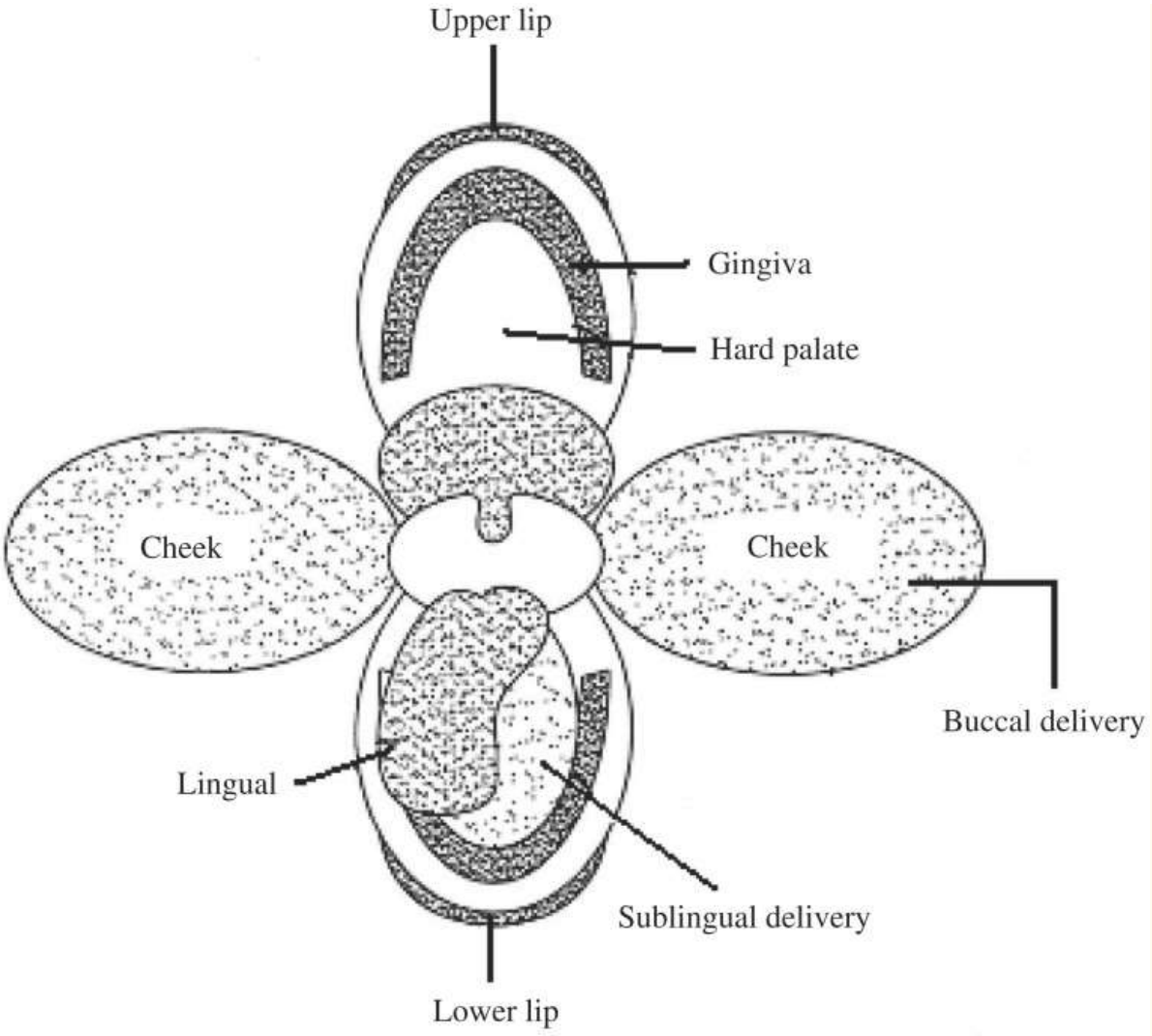
The mucosal linings of the nasal, rectal, vaginal, ocular, and oral cavities, which are collectively referred to as the "transmucosal routes of drug delivery," present fantastic possibilities and possible advantages over peroral administration for the delivery of systemic drugs. These mucosal linings are known as the "transmucosal routes of drug delivery." Oral drug administration has a number of advantages over parenteral administration, including a more favourable enzymatic flora for drug absorption, as well as the potential to prevent the first pass effect and presystemic clearance within the gastrointestinal tract.

There are two main types of drug distribution in the oral mucosa;

a) Buccal delivery

b) sublingual delivery

Because of how easily it can be reached, the buccal mucosa of the mouth is an excellent location for the delivery of drugs. Buccal medication delivery is the practise of giving a drug via the buccal mucosal membrane that lines the mouth cavity. This method is also referred to as "mouth medication delivery." This method of administering a medicine is effective at creating mucosal (local impact) as well as transmucosal (systemic effect) effects simultaneously. With regard to the first, the objective is to achieve mucosa-specific drug release; with regard to the second, the drug must be absorbed through the mucosal barrier and into the bloodstream. When compared to tablet and capsule formulations, buccal formulations have the possibility for a considerably lower drug concentration, which means that the likelihood of toxicity or other undesirable side effects is also lowered by using buccal formulations .[1]



1.2 Buccal Dosage Form Classification:

1.Tablets with buccal bioadhesion.

2. Semisolid buccal bioadhesives.

3. Films and patches with buccal bioadhesive.

4. Powders for buccal bioadhesion.

1. Buccal Tablets: These oral dose forms are dry, they require a little bit of water to be added to them before they can be applied to the buccal mucosa. At the moment, double and multilayered tablets are created by using bioadhesive polymers and excipients in the formulation process. Compressing powder into a solid form results in the formation of tablets similar to these. Depending on the excipients that were employed, dosage forms may either adhere to the mucosal surface or dissolve while the patient is chewing them. A number of different methods can be utilised to bring medication to the mucosal surface of the mouth.[1]

2. Buccal Bioadhesive Lyophilized Dosage Forms: Natural or synthetic polymers, such as arabase, are dispersed in polyethylene or an aqueous solution in order to produce mucosa bioadhesive semisolid dosage forms.

3. Mucosa Bioadhesive Patches and Films: To guarantee that the medicine is absorbed evenly throughout the buccal mucosa, buccal bioadhesive patches can either be round or oval in shape and made of a two-ply laminate or a multilayered thin film. Dissolving medicines in the alcohol solution of the bioadhesive polymer is the first step in the production of buccal bioadhesive films.[1]

4. Dosage Forms of Buccal Bioadhesive Powder: Bioadhesive polymers and the medication are combined in buccal bioadhesive powder dosage forms.[1]

1.3 Ideal Characteristics of Buccal Drug Delivery:

An ideal BDDS should have following characteristics:

- Well moisturized, soluble and biodegradable
- Polymer and its decaying derivatives should be harmless and free from leaching toxins.
- Should have good adhesive properties and mechanical strength.
- Bio-adhesive set should be ductile and have firmness.
- Polymer should be readily accessible and cost-effective.
- Should demonstrate both dry and liquid bio-adhesive properties.
- If inhibition and penetration properties in local enzymes are shown, they should have adhesively active groups.
- Molecular weights should be optimal.
- Must indicate acceptable shelf-life.
- Spatial confirmation is necessary.
- Should havegood bonding nature.
- Should stick for few hours to the attachment site.
- Subject to controlled release of the medication
- Should have unidirectional drug release into the mucosa
- Should effectively enhance absorption rate and duration of medication.
- Should not irritate patient or trigger any discomfort
- Should not affect basic processes such as speaking and drinking[2]

1.4 Mechanism OF BDDS :

Drug delivery through oral mucosa: After delivery of a medicine sublingually, buccally, or locally, it may be feasible for the medication to be absorbed through the mucous membranes of the mouth. When referring to all geographic places that do not fall into the first two categories, the term "local region" is used. On the basis of the thickness of the tissues and the quantity of keratinization they contain, the oral mucosa is often considered to be an epithelium that has a high level of permeability, with a permeation rank order that goes as follows: sublingual > buccal > palatal.[3]

BUCCAL PATCHES

The buccal patch is an example of a non-dissolving fine matrix modified-release dose form. It is made up of one or more polymer films or layers that contain the medication and/or other excipients. Delivery of medications through the buccal route has the potential to significantly boost their bioavailability. Because of the abundant vascularity of the buccal mucosa, it is possible for medications to enter the general bloodstream of the body without first having to pass through the digestive system.

Plus, buccal tablets and gum. so that the drug's absorption can be rapidly halted if a negative reaction occurs. Some patches are more adaptable than tablets, gels, or other buccal administration forms. Comfortable.[4]

2. Sustained release drug delivery system:

A steady state level in the blood that is effective in treatment and non - toxic for a long time is the fundamental aim of treatment. The layout of Using the correct dosage schedules is crucial to achieving this objective. Continued release, continued action, timed, controlled release, and prolonged action.

designed to release medication continuously for a long time after administration to prolong the therapeutic effect one dosage. If the dosage form is an injectable, this time frame is expressed in hours. Depending on the dosage form's residence time

gastrointestinal system. CR stands for controlled release has started to be connected to those systems from which medications are potentially automatically delivered over time at predetermined rates in time. These kinds of products have been created. For topical, injectable, and oral use, as well as insert insertion into bodily cavities.

Any drug delivery method that achieves a slow release of the drug through a prolonged period is considered a sustained release system. A controlled release system is one that successfully maintains continuous drug levels in the blood or target tissue. It is referred to as a prolonged release structure if it fails to accomplish this but still prolongs the action duration beyond what is possible with conventional delivery. Due to increased design flexibility for dosage forms, the oral route of intake for sustained drug release systems has drawn more attention. The type of delivery mechanism, the illness being treated, the patient, the length of therapy, and other important

interrelated factors are all taken into consideration when designing oral sustained release delivery systems.[5]

3. Preformulation studies:

Preformulation can be defined as the study of the physical and chemical properties of pharmaceuticals before to formulation, as the name suggests, where Pre means before and formulation means to formulate/develop the substance.[6]

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Study of some physicochemical parameters: There are several parameters that are to be studied before development of any formulation.

3.1. Organoleptic properties
3. 2. Melting point
3. 3. IR for Identification
3.4. Preparation of Calibration curve of the drug
3.5. Solubility
3.6. Partition coefficient. [6]

Organoleptic Properties: Basically, it refers to the process of identifying a substance through taste, sight, smell, and touch. Shape, colour, odour, and taste are examples of the qualities. Descriptive nomenclature for paroxetine's colour, smell, and taste was also investigated. [6]

Melting point determination: includes figuring out the temperature at which a medication transitions from a solid to a liquid state. After placing the sample inside a capillary, seal the opening by putting the capillary over a flame for two to three minutes. The capillary was filled with the sample and then put into the melting point device. The temperature at which a medication changes from one state to another is known as its melting point. [6]

IR for identification of drug:

The FTIR spectra of the sample and the standard drug were compared in order to identify the drug molecule. The KBr pellet method was used to identify the medication.[7]

Determination of solubility: Determination of drug solubility in various solvents (water, methanol, chloroform). A saturated solution was made by adding 5–10 ml of solvent to a beaker containing a little quantity of medicine. The samples were filtered, diluted, and checked for the presence of any undissolved particles after being kept at room temperature for 24 hours. [7]

Table 1: Parameters of Solubility as per I.P

S.NO	Descriptive Term	Parts of solvent required for one part of solute
1.	Very Soluble	Less than 1
2.	Freely Soluble	From 1 to 10
3.	Soluble	From 10 to 30
4.	Sparingly Soluble	From 30 to 100
5.	Slightly Soluble	From 100 to 1,000
6.	Very Slightly Soluble	From 100 to 1,000
7.	Practically insoluble	From 100 to 1,000

4. Composition of buccal patches : The patches were prepared by solvent casting method. four patches of paroxetine were prepared using several polymers, permeation enhancers, plasticizers etc. Generally, a solution of drug was prepared in a beaker and on the other hand in a beaker the polymers were dissolved in the solvent and in that the other ingredients like permeation enhancers, plasticizers were added and mixed very well. The solution of drug was than mixed into the polymeric solution. At this point a viscous solution is obtained which was then poured on a clean petri plate. It was left to dry for 24 hrs and after 24 hrs the dried patches were collected and evaluated. [8]

Fig 1: Formulation of patche

5. RESULT DISCUSSION

Evaluation parameters: The parameters that are studied to evaluate the prepared patches are:

1. Thickness of the patch
2. Appearance
3. Weight uniformity
4. Folding endurance
5. Percent moisture content
6. In-vitro diffusion study
7. % Moisture uptake
8. Drug content

1. THICKNESS: Using a vernier calliper, the patch's thickness was measured, and the average of three measurements was computed.[9]

2. APPEARANCE: The colour, shape of the film was observed by keeping the film in the presence of light.[9]

3. FOLDING ENDURANCE :A strip of approximately 1 cm by 1 cm was cut from a precise location and folded repeatedly at the same spot until it broke. The number of times the film was folded at the same location without breaking gives the folding endurance rating.[10]

4. WEIGHT UNIFORMITY: Randomly selected patches were dried and weighed accurately using electronic balance and average weight and % weight variation was calculated.[9]

% Weight variation= (Individual weight/Average weight)*100%

5. PERCENT MOISTURE CONTENT: The patches are first weighed at room temperature (W1), then placed in a desiccator with silica for 24 hours. The patches are then reweighed, taking into account the final weight (W2), a nd the percentage of moisture content is determined by dividing the initial and final weight differences by the final weight and multiplying by 100.[11]

% Moisture content= {(Initial weight – Final weight)/ Final weight}* 100%

6. Drug Content: The film was chopped into small pieces and dissolved in a specific amount of solvent or buffer. Spectrophotometric analysis was used to measure the absorbance.[10]

7. Percent moisture Uptake: Films that had been precisely weighed were stored in a desiccator with sodium chloride solution at 845 RH for 24 hours. After that, the films were reweighed, and the percentage of moisture uptake was determined by multiplying the initial weight by the final weight difference.[11]

% Moisture uptake= {(Final weight- Initial weight)/Initial weight}*100%

6. Preformulation studies:

6..1 ORGANOLEPTIC PROPERTIES:

S.NO	PROPERTIES	OBSERVATION
1.	COLOUR	White
2.	ODOUR	Odourless
3.	TASTE	Bitter

DISCUSSION: From table no it is found that organoleptic properties of test drug matches with the standard drug.

6.2. MELTING POINT:

S.NO	OBSERVED M.P.	AVERAGE M.P.	STANDARD M.P.
1.	132		
2.	130	132.6	135-137
3.	136		

DISCUSSION: From table it is found that the melting point of the sample drug is very close to the standard drug.

6.3. SOLUBILITY:

S.NO	SOLVENTS	SOLUBILITY	OBSERVATION
1.	WATER		Poorly soluble
2.	ETHANOL		
3.	PHOPHSTE BUFFER		

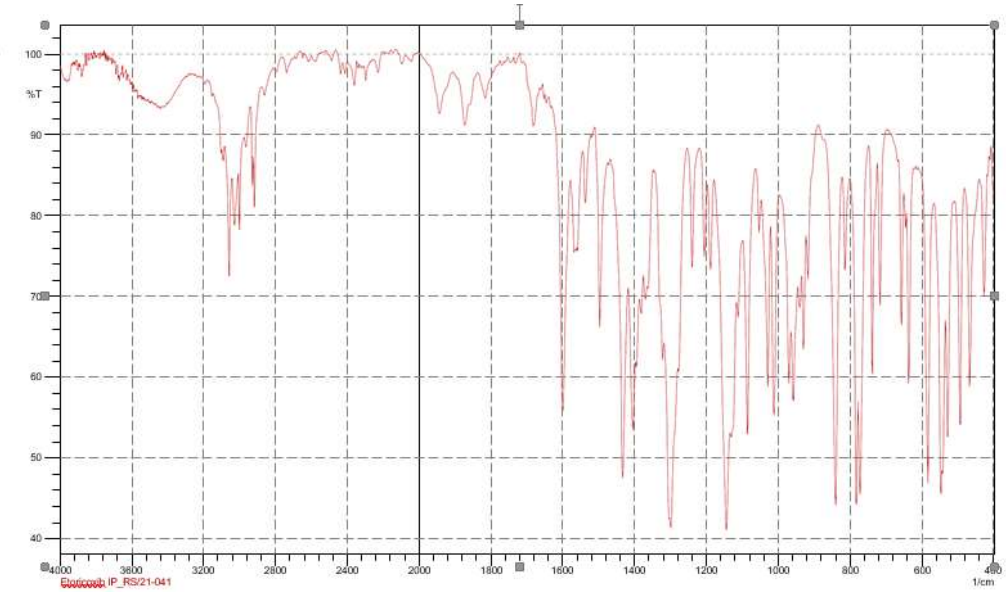
DISCUSSION: From table it is very clearly seen that the drug sample is poorly soluble in water

6.4. PARTITION COFFICIENT:

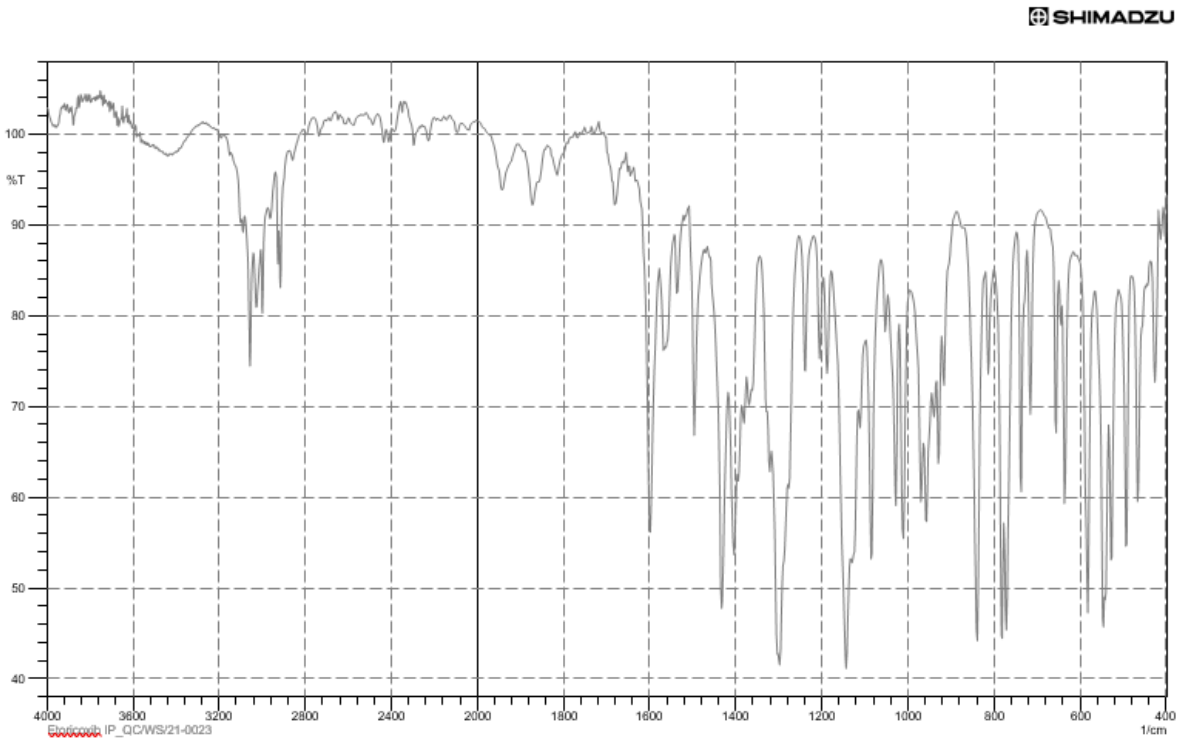
S.NO	OBSERVED VALUE	STANDARD VALUE
1.	1.87	3.9

DISCUSSION: From table it is observed that the partition coefficient of the sample is very similar to the standard value.

6.5. FTIR STUDIES:



Observed IR OF the Sample

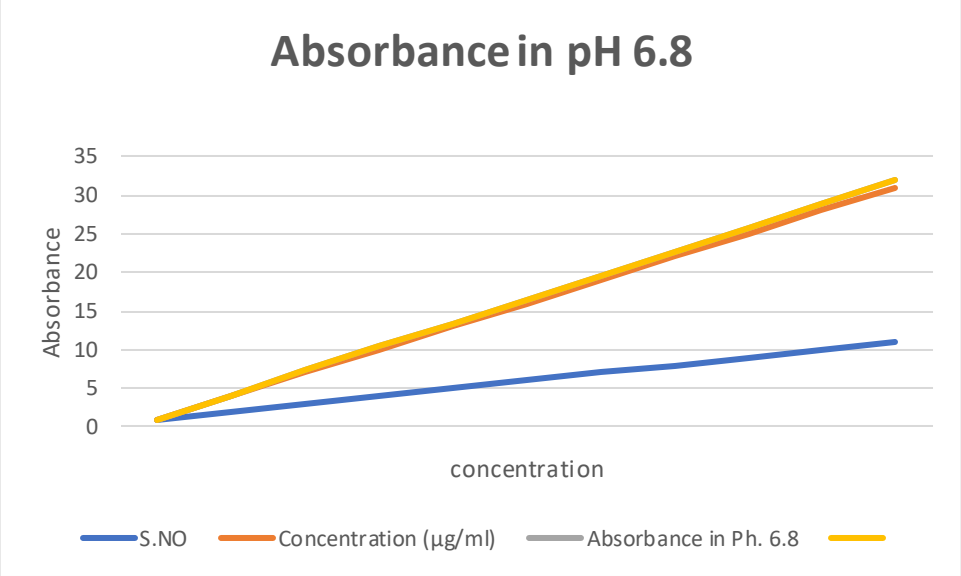


Standard cure of Etoricoxib

6.6.CALIBRATION CURVE

S.NO	Concentration (µg/ml)	Absorbance in Ph. 6.8
1	0	0

2	2	0.122
3	4	0.238
4	6	0.378
5	8	0.416
6	10	0.484
7	12	0.575
8	14	0.653
9	16	0.764
10	18	0.801
11	20	0.875



6.7. EVALUATION STUDIES:

. APPERANCE:

S.NO	FORMULATION	RESULT
1.	F1	Transparent, non-sticky
2.	F2	Transparent, non-sticky
3.	F3	Transparent, non-sticky
4.	F4	Transparent, non-sticky
5.	F5	Transparent, non-sticky
6.	F6	Transparent, non-sticky

DISCUSSION: The appearance of the patches were all similar i.e. Transparent and non-sticky.

Thickness:

S.NO	FORMULATION	THICKNESS (mm)
1.	F1	0.17±0.02
2.	F2	0.11±0.04

3.	F3	0.14±0.01
4.	F4	0.17±0.04
5.	F5	0.33±0.03
6.	F6	0.27±0.04

DISCUSSION: The thickness of the patches was in the range of 0.17±0.02mm to 0.33±0.03mm. The patches were found to be in a consistent thickness.

6.8 Weight Variation:

S.NO	FORMULATION	WEIGHT VARIATION(±S.D.) in gm
1.	F1	0.285±0.01
2.	F2	0.257±0.01
3.	F3	0.305±0.004
4.	F4	0.310±0.001
5.	F5	0.326±0.030
6.	F6	0.314±0.0010

DISCUSSION: The average weight of film was found to range between 0.285±0.01to 0.326±0.03. The weight variation appears to be within as per I.P

6,9 . PERCENT MOISTURE CONTENT:

S.NO	FORMULATION	RESULT(±S.D.) in %
1.	F1	2.88±0.16
2.	F2	4.13±0.117
3.	F3	4.09±0.024
4.	F4	3.96±0.044
5.	F5	6.13±0.31
6.	F6	5.23±0.047

DISCUSSION: The % moisture content of the drug ranges between 6.13±0.31 to 2.88±0.16.

6.10 DISINTEGRATION TIME:

S.NO	FORMULATION	DISINTEGRATION TIME (Sec)
1.	F1	21
2.	F2	28
3.	F3	14
4.	F4	31
5.	F5	20
6.	F6	34

DISCUSSION:. It was seen that formulation F3 was disintegrated in 14 secs and formulation F6 was disintegrated in 34 secs.

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6.11. DRUG CONTENT:

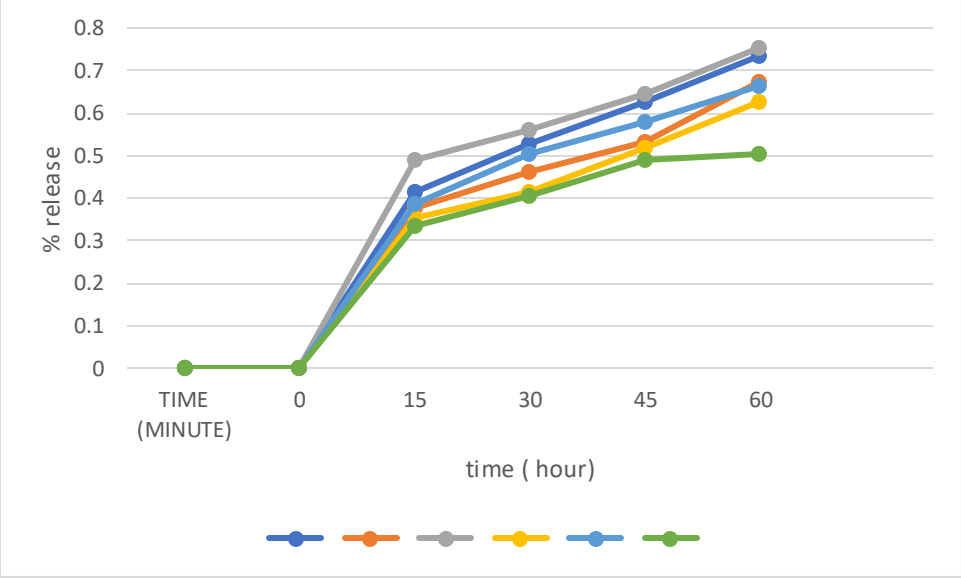
S.NO	FORMULATION	% DRUG CONTENT

1.	F1	98.33±0.13
2.	F2	92.55 ± 0.18
3.	F3	97.56± 0.14
4.	F4	93.41±0.16
5.	F5	94.66±0.11
6.	F6	97.25±0.14

DISCUSSION: From table no- 27.It is clearly seen that the drug content ranges from 92.55 ± 0.18 to 98.33±0.13

6.12 . IN-VITRO DISSOLUTION TEST: The in-vitro release of the drug was done by using USP Type-II apparatus, maintaining the temperature at 37±0.5°C and rotating with the speed of 50rpm in 300 ml of simulated salivary fluid having Ph 6.8

TIME (MINUTE)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
0	0	0	0	0	0	0
15	41.67%	37.54%	48.86%	35.52%	38.65%	33.55%
30	52.65%	46.32%	55.97%	41.33%	50.43%	40.65%
45	62.54%	53.23%	64.34%	51.75%	57.74%	48.87%
60	73.32%	67.56%	75.23%	62.43%	66.45%	50.56%



DISCUSSION: F3 shows maximum release of drug having appropriate level of polymer added in the film. And the drug release was not so good in Formulation F6 having higher concentration of polymer in it. So the formulation F3 is considered for better rate of drug release as compared to other formulation.

7. CONCLUSION

All of the transdermal film formulations were observed to be satisfactory, with no signs of breaking or cracking. The use of HPMC, pectin provides the requisite controlled release property. That is why they were chosen as a polymer for the formulation of transdermal film. several post-formulation evaluation studies such as folding endurance, moisture uptake thickness, weight Variation, moisture percentage, and drug content, the formulated transdermal film provided satisfactory results. film can be produced to reduce dosage time and increase bioavailability by adding a penetration enhancer into the formulation. More research is needed to determine the efficacy of these formulations and the appropriate dose.

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