FORMULATION OPTIMIZATION AND EVALUATION OF FAST MOUTH DISSOLVING FILM OF DICLOFENAC SODIUM BY SOLVENT CASTING METHOD

Puja R. Manale[1], Mrunal Shirsat[1], Santosh Tarke[1], Naresh Jaiswal.[1], I. J. Singhvi[2]

[1] SBSPM B-Pharmacy College Ambajogai

[2] Nootan College of Pharmacy, Sankalchand Patel University, Visnagar

Corresponding Author Details:Puja R. Manale

pujamanale1996@gmail.com

ABSTRACT

Fast dissolving drug delivery systems such as mouth dissolving films (MDF) are novel dosage forms that disintegrate or dissolve within the oral cavity. These offer a convenient way of dosing medications, not only to special population groups with swallowing difficulties such as children & the elderly, but also to the general population.Mouth dissolving film (MDFs) is the latest oral solid dosage form because of its easy to use properties. When mouth dissolving films are placed in mouth, it disintegrates & dissolves within a minute without consuming water or chewing. This dosage form has added advantage as it allows the medication to bypass the first pass metabolism, so bioavailability of medication may be enhanced. Mouth dissolving film has capability to enhance onset of action, lower the dosing eliminate the fear of chocking.

Diclofenac Sodium is a NSAID. Diclofenac is a medicine that reduces swelling (inflammation & pain). It is used to treat aches & pain as well as problems with joints, muscles & bones. It is also used to tread rheumatoid arthritis. In the present study, total nine formulations by solvent casting method using polymer- hydroxy propyl methyl cellulose & plasticizer- PEG 6000 are prepared & evaluated.The prepared films were evaluated for various parameters like physical appearance thickness, weight variation, and time, Surface PH, folding endurance, percentage moisture loss, Disintegration time, In vitro wetting time, mouth dissolving time & drug content uniformity. from the evaluations, it was found that F2 batch was ideal fast dissolving as the film was nicely formed.

Keywords: Fast Dissolving Film, HPMC, PEG6000, Solvent Casting Method, Diclofenac Sodium.

INTRODUCTION:

The oral route of administration have always been preferred over the other routes of administration namely, parenteral, topical, rectal and vaginal by the medical practitioners, manufacturers due to patient acceptance (1, 2).Ease of administration, convenience and cost effectiveness has been the reason behind the popularity of this route among the patient population (1, 3). The oral cavity has unique environment that offers its potential as a site for drug delivery (2). There has been a lot of advancement in the oral solid drug delivery system, from conventional dosage forms such as tablets and capsules to modified release dosage forms and recently the fast dissolving dosage forms (Fig1.1).Ease of administration, convenience and cost effectiveness has been the reason behind the popularity of this route among the patient population (1, 3).The limitation of difficulty in swallowing oral solid dosage forms has been the reason for the evolution of mouth dissolving drug delivery system.

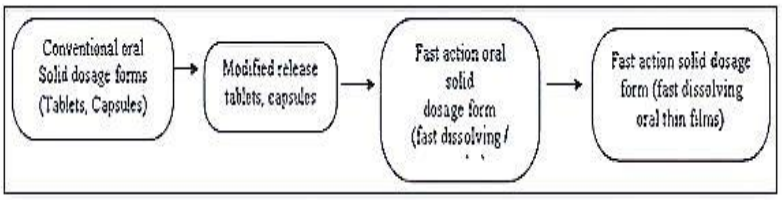


Figure No.1 Stages in the Development of Oral Dosage Forms (1)

Mouth Dissolving films are oral solid dosage forms that disintegrate and dissolve when placed in the mouth without taking water (2). Mouth dissolving films are gaining popularity and acceptance among the pediatric, geriatric and dysphagia patients who fear choking. Mouth dissolving films provides convenience, ease of administration and faster onset of action, as the drug is absorbed through oral mucosa and enters the systemic circulation, bypassing the first pass metabolism.

Classification Of Fast Dissolve Technology:

Fast dissolve technologies can be divided into three broad groups:

I. Lyophilized systems,
II. Compressed tablet-based systems,
III. Thinfilmstrips.

Classification of Oral Film:

There are three different sub types

(1)Flash release,
(2)Mucoadhesive melt-away wafer,
(3)Mucoadhesive sustained-release wafers.

NSAIDs

Nonsteroidal anti-inflammatory medications (NSAIDs) are pharmaceuticals that have analgesic, antipyretic, and anti-inflammatory actions, as they lower pain, fever, and inflammation. The term "non-steroidal" is used to separate these medications from steroids, which have a similar eicosanoid-depressing, anti-inflammatory action (among many other effects). NSAE)s are non-narcotic analgesics, as opposed to opioid analgesics. Nonsteroidal anti-inflammatory agents/analgesics (NSAIAs) or nonsteroidal anti-inflammatory medications (NSAIMs) are other names for NSAIDs. Aspirin, ibuprofen, diclofenac, indomethacin, and naproxen are the most well-known members of this class of medicines. NSAIDs have become an important aspect of the pharmacological treatment of pain (at low dosages) and inflammation (at higher levels) since the extraction of salicin from the folk medicine willow bark in 1829. NSAIDs are popular because, unlike opioids, they do not cause drowsiness or respiratory depression and have a very low addiction rate. NSAIDs, on the other hand, have their own set of issues (see below).

Certain NSAIDs, such as ibuprofen and aspirin, have gained acceptance as reasonably safe and are now accessible without a prescription over-the-counter.

Material and Method

Materials

Drug

Diclofenac sodium is obtained from Research Lab Finechem. Industries. & all other chemicals (i.e. HPMC &PEG) are obtained from Research Lab Finechem. Industries. **Excipients**:The excipients employed in formulation development are listed in table.

Table No1: List of excipients used in formulation

Sr. no	Drug/Excipient	Manufacturer/Supplier
1	Diclofenac Sodium	Research Lab Finechem Industries
2	Polyethylene glycol 6000	Research Lab Fine chem Industries
3	Hydroxy propyl Methyl Cellulose	Research Lab Fine chem Industries

Equipments

Instruments and equipments used during the course of the project are listed in table.

Chemicals: Chemicals and reagents employed for the preparation of buffers, analytical solutions and other experimental purposes are listed in table

Table No2 : Chemicals and reagents utilize in formulation and development study

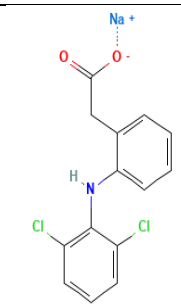
Sr. no	Chemical	Supplier/ Manufacturer
1	Potassium Dihydrogen Phosphate	New tech Pharma Healthcare, Ambajogai
2	Disodium Hydrogen Phosphate	New tech Pharma Healthcare, Ambajogai
3	0.1% w/v Amaranth Red Solution	New tech Pharma Healthcare, Ambajogai
4	Anhydrous Calcium Chloride	New tech Pharma Healthcare, Ambajogai
5	Distilled Water	SBSPM College,Ambajogai

Drug & Excipient Profile:

A. Drug Profile:

1. Diclofenac Sodium

Drug Name	Diclofenac Sodium
IUPAC Name	sodium;2-[2-(2,6-dichloroanilino)phenyl]acetate
Molecular Formula	$C_{14}H_{10}Cl_2NNaO_2$
Molecular weight	318.1 g/mol

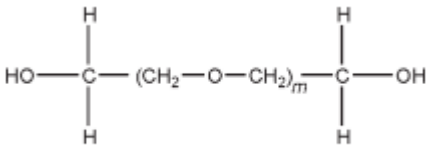
Structure	 **Structure of Diclofenac sodium**
CAS No.	15307-79-6
Synonym	Diclofenal Diclofenac Diclofenac Potassium Diclofenac Sodium Diclonate P Diclophenac Dicrofenac Feloran GP-45,840 Novapirina
Solubility	Water solubility 0.00482 mg/mL
Background	A drug that is used to treat the symptoms of rheumatoid arthritis and is being studied in the prevention and treatment of some types of skin cancer. It blocks substances that cause inflammation and pain. It may also prevent the growth of new blood vessels that tumors need to grow.
Pharmacodynamics	Diclofenac sodium acts by potent cyclo-oxygenase inhibition, reduction of arachidonic acid release, and enhancement of arachidonic acid uptake. It thereby results in a dual inhibitory effect on both the cyclo-oxygenase and lipoxygenase pathways.
Mechanism of action	As with all NSAIDs, diclofenac exerts its action via inhibition of prostaglandin synthesis by inhibiting cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) with relative equipotency.
Absorption	Diclofenac is 100% absorbed after oral administration compared to IV administration as measured by urine recovery. However, due to first-pass metabolism, only

	about 50% of the absorbed dose is systemically available (see Table 1). Food has no significant effect on the extent of diclofenac absorption.
Protein binding	It has been reported that diclofenac, 2-arylacetic acid, a non-steroidal anti-inflammatory drug binds to human plasma protein12. Existence of two classes of binding sites has been reported on human serum albumin for diclofenac sodium13.
Metabolism	Diclofenac is eliminated following biotransformation to glucoroconjugated and sulphate metabolites which are excreted in urine, very little drug is eliminated unchanged. The excretion of conjugates may be related to renal function.
Route of elimination	Diclofenac is mainly eliminated via metabolism. Of the total dose, 60-70% is eliminated in the urine and 30% is eliminated in the faces. No significant enterohepatic recycling occurs. The terminal half-life of diclofenac is approximately 2 h, however the apparent half-life including all metabolites is 25.8-33 h.
Half-life Period	Diclofenac sodium was excreted with an average half-life of 1.15 h.
Toxicity	Taking too much diclofenac sodium does not usually cause serious problems. The person may have some stomach pain and vomiting (possibly with blood). However, these symptoms will likely get better. In rare cases, a blood transfusion is needed.

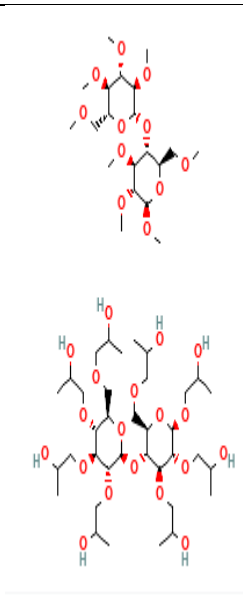
Excipient Profile:

1. Polyethylene Glycol 6000:

Excipient Name	**Polyethylene Glycol 6000**
Synonyms	Carbowax; Carbowax Sentry; Lipoxol; Lutrol E; macrogola; PEG; Pluriol E; polyoxyethylene glycol.

Chemical Name	a-Hydro-o-hydroxypoly(oxy-1,2-ethanediyl)
CAS Registry Number	[25322-68-3]
Empirical Formula	H(OCH2CH2)nOH
Solubility	*Soluble in water (500 g/l at 20° C), aromatic hydrocarbons (very), and aliphatic hydrocarbons (slightly).*
Structural Formula	 **Structure of PEG 6000**
Functional Category	Ointment base Plasticizer Solvent suppository base tablet and capsule lubricant
Applications	Polyethylene glycol grades with molecular weights of 6000 and above can be used as lubricants, particularly for soluble tablets. The lubricant action is not as good as that of magnesium stearate, and stickiness may develop if the material becomes too warm during compression. An antiadherent effect is also exerted, again subject to the avoidance of overheating. Polyethylene glycols have been used in the preparation of urethane hydrogels, which are used as controlled-release agents. Polyethylene glycol has also been used in insulin-loaded microparticles for the oral delivery of insulin;(49,50) it has been used in inhalation preparations to improve aerosolization;(51) polyethylene glycol nanoparticles have been used to improve the oral bioavailability of cyclosporine;(52) it has been used in self-assembled polymeric nanoparticles as a drug carrier;(53) and copolymer networks of polyethylene glycol grafted with poly(methacrylic acid) have been used as bioadhesive controlled drug delivery formulations.(54)

2. Hydroxy Propyl Methyl Cellulose:

Excipient Name	**Hypromellose**
Synonyms	Benecel MHPC; E464; hydroxypropyl methylcellulose; HPMC; hypromellosum; Methocel; methylcellulose propylene glycol ether; methyl hydroxypropylcellulose; Metolose; MHPC; Pharmacoat; Tylopur; Tylose MO.
Chemical Name	Cellulose hydroxypropyl methyl ether
CAS Registry Number	9004-65-3
Empirical Formula	$C_{56}H_{108}O_{30}$
Solubility	This product is soluble in water (10 mg/ml).
Structural Formula	 **Structure of Hypromellose**
Functional Category	Bioadhesive material; coating agent; controlled-release agent; dispersing agent; dissolution enhancer; emulsifying agent; emulsion stabilizer; extended-release agent; film-forming agent; foaming agent; granulation aid; modified-release agent; mucoadhesive; release-modifying agent; solubilizing agent; stabilizing agent; suspending agent; sustained-release agent; tablet binder; thickening agent; viscosity-increasing agent.
Applications	Hypromellose is widely used in oral, ophthalmic, nasal, and topical pharmaceutical formulations. In oral products, hypromellose is primarily used as a tablet binder,(55) in film-coating,(56–61) and as a matrix for use in extendedrelease tablet formulations.(62–86) Concentrations between 2% and 5% w/w may be used as a binder in either wet- or dry-granulation processes.

	High-viscosity grades may be used to retard the release of drugs from a matrix at levels of 10–80% w/w in tablets and capsules. Hypromellose is also used in liquid oral dosage forms as a suspending and/or thickening agent at concentrations ranging from 0.25–5.0%.(67) Depending upon the viscosity grade, concentrations of 2–20% w/w are used for film-forming solutions to film-coat tablets. Lower viscosity grades are used in aqueous film-coating solutions, whilehigher-viscosity grades are used with organic solvents. Examples of film-coating materials that are commercially available include AnyCoat C, Spectracel, Pharmacoat, and the Methocel E Premium LV series.

Method:-A. Pre formulation of Diclofenac Sodium: I. Construction of Calibration curve of Diclofenac sodium:

Initially prepare a standard stock solution of Diclofenac sodium by accurately weighing 100 mg of Diclofenac Sodium in 100 ml Volumetric flask and add 70 ml of Phosphate buffer pH 6.8 and shake to dissolve the drug and make up to the mark with same solvent. Further make a series of dilution by pipetting 1, 2, 3, 4, 5, 6, 7, 8, and 9 ml of standard stock solution in individual 10 ml volumetric flasks and make up to the mark with phosphate buffer pH 6.8 to prepare the concentration of 10, 20, 30, 40, 50, 60, 70, 80 and 90 µg/ml respectively and measure the absorbance of these solutions at 296 nm using double beam UV Spectrophotometer.

B.Formulation of fast dissolving film of Diclofenac Sodium:

Fast dissolving film of Diclofenac Sodium was developed by solvent casting method using film forming polymer such as HPMC & Other film modifiers such as PEG 6000, etc.

Above those two are weighed accurately & soaked with water simultaneously the required amount of Diclofenac sodium id dissolved in sufficient quantity of water. This prepared solution were added to the previously prepared polymeric solution & mixed well to get homogenous solution followed by other excipients. This homogenized solution is kept for 24 hrs. at room temperature for evaporation of solvent after complete evaporation of solvent, films were obtained & the resultant film was cut into the uniform dimension (2 cm X2 cm), which were then wrapped in a aluminums foil & stored in a desiccator.

Evaluation parameters

1) Physical appearance: The prepared films were visually inspected for color, clarity & flexibility and smoothness.
2) Thickness: The thickness of every oral film was determined at five different places using screw gauge. The average thickness & standard deviation of thickness of each film formulation was determined.
3) Weight variation:2 cm X 2cm films were cut at 5 different places & weight of each film was taken on an electronic balance & the average weight and standard deviation was calculated.

4) Surface pH: The surface pH of fast dissolving film was determined in order to investigate the possibility of any side effects with vivo. The films were allowed to smell in closed petri-dish containing 0.5 ml phosphate buffer. At room temperature for 30 minutes & the pH was determined with digital pH meter.

5) Folding Endurance Test: The folding endurance was determined by folding the film (2 cm X 2 cm) at the same place repeatedly until it broke. The folding endurance was measured by calculating the number of times the film folded. At the same place without breaking or cracking.

6) Percentage moisture loss: This was determined by keeping the fast dissolving films in a desiccator containing anhydrous calcium chloride after 24 hrs.The films were taken out & the % moisture loss was calculated using the formula.

7) Disintegration time: In vitro D.T. was determined visually in a beaker which contains 25 ml of phosphate buffer (pH 6.8) with swirling every 10 sec. the disintegration time is the time when the film stats to break or disintegrate.

8**) In Vitro Wetting Time:** A circular paper was placed in the petriplate. 6 ml of 0.1 % W/V Amaranth dye solution was prepared& added to the petriplate. The film strip (2 cm X2 cm) was placed on the surface of tissue required for the dye to appear on the surface of the film was noted as a wetting time.

9) **Mouth dissolving time:** The mouth dissolving time was determined by placing the film manually into phosphate buffer. The time required by the film to dissolve was noted.

10) **Drug content uniformity**: The drug content was determined by dissolving the film of 4 cm^2 in 100 ml phosphate buffer (6.8 pH) Using magnetic stirrer for 30 min. & the drug content was evaluated spectrophotometrically at 296 nm & Average was taken.

RESULT & DISCUSSION:

Preformulation Studies:

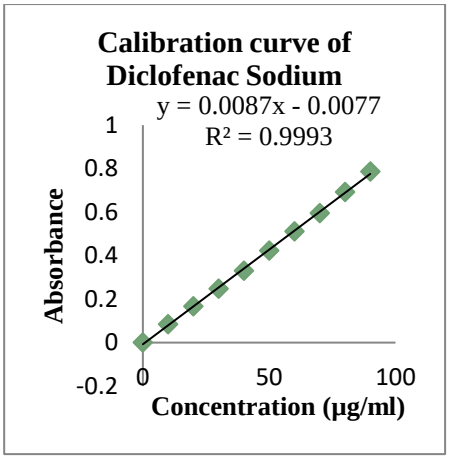
Calibration curve of Diclofenac Sodium:

The Calibration curve of Diclofenac sodium was constructed using Phosphate buffer pH 6.8 in the concentration range from 10 to 90 µg/ml. The Results of Calibration curve are given in Table 3.1.

Table No3 : Results of Calibration curve

Concentration (µg/ml)	Absorbance at 296 nm
0	0.0000
10	0.0843
20	0.1677
30	0.2481
40	0.3301
50	0.4229
60	0.5123
70	0.5956
80	0.6931
90	0.7862

The Calibration curve of Diclofenac sodium was constructed by plotting Concentration Vs Absorbance obtained at 296 nm. The Calibration curve is given in Figure 7.1. The Regression coefficient was found to be 0.9993.



Formulation of Diclofenac Sodium Fast Dissolving Film:

9 formulations of Diclofenac Sodium Fast Dissolving film was prepared by varying concentration of HPMC and PEG 6000 and 100 mg Diclofenac sodium was added in all the formulations. The Detailed formulation table is given in Table 3.2.

Table No 4: Formulation Table for Diclofenac Sodium Fast Dissolving Film

Sr. No.	HPMC (gm)	PEG 6000 (gm)	Dichlofenac sodium (gm)
1	0.250	0.1	0.1
2	0.625	0.1	0.1
3	1.000	0.1	0.1
4	0.250	0.3	0.1
5	0.625	0.3	0.1
6	1.000	0.3	0.1
7	0.250	0.5	0.1
8	0.625	0.5	0.1
9	1.000	0.5	0.1

Optimization of Diclofenac sodium Fast Dissolving Film:

The optimization of Diclofenac sodium fast dissolving film wasdone by using central composite design. Following are the details of the optimization of fast dissolving film.

Independent variable	Unit	Lower Value (-1)	Normal Value (1)	Higher Value (+1)
HPMC	Gms	0.25	0.625	1
PEG 6000	Gms	0.1	0.3	0.5

The effect of HPMC and PEG 6000 concentration on in-vitro wetting time and mouth dissolving time were evaluated.

In-vitro Wetting Time:Table: ANOVA for 2FI Model

Source	Sum of Squares	Df	Mean Square	F-Value	p-value	
Model	83.41	3	27.80	5.23	0.0532	Not significant

A-HPMC	25.04	1	25.04	4.71	0.0822	
B-PEG 6000	22.45	1	22.45	4.22	0.0951	
AB	34.37	1	34.37	6.46	0.0518	
Residual	26.59	5	5.32			
Cor Total	110.00	8				

The Model F-value of 5.23 implies there is a 5.32% chance that an F-value this large could occur due to noise. P-values less than 0.0500 indicate model terms are significant. In this case there are no significant model terms. Values greater than 0.1000 indicate the model terms are not significant.

Table No 5: Fit Statistics

Std. Dev.	2.31	**R^2**	0.7583
Mean	32.67	**Adjusted R^2**	0.6132
C.V. (%)	7.06	**Predicted R^2**	0.0555
		Adeq Precision	6.4659

The Predicted R^2 of 0.0555 is not as close to the Adjusted R^2 of 0.6132 as one might normally expect; i.e. the difference is more than 0.2. This may indicate a large block effect or a possible problem with your model and/or data. Things to consider are model reduction, response transformation, outliers, etc. All empirical models should be tested by doing confirmation runs. Adeq Precision measures the signal to noise ratio. A ratio greater than 4 is desirable. The ratio of 6.466 indicates an adequate signal. This model can be used to navigate the design space.

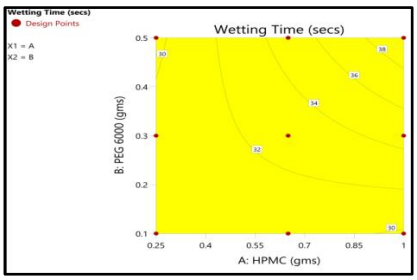


Figure 1: Contour Plot of Wetting time HPMC Vs PEG 6000

As the Concentration of PEG 6000 and HPMC increases, the in-vitro wetting time also increases. Lower concentration of HPMC and higher concentration of PEG 6000 leads to lower in vitro wetting time.

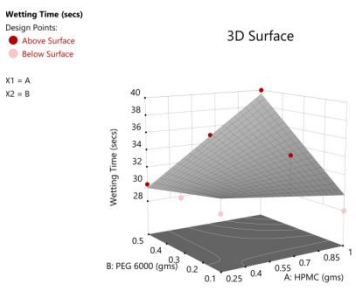


Figure2: 3D Contour Plot

Mouth Dissolving Time:
Table: ANOVA for 2FI Model

Source	Sum of Squares	Df	Mean Square	F-Value	p-value	
Model	134.32	2	67.16	3.20	0.1133	Not significant
A-HPMC	53.65	1	53.65	2.56	0.1609	
B-PEG 6000	80.67	1	80.67	3.84	0.0976	
Residual	125.90	6	20.98			
Cor Total	260.22	8				

The Model F-value of 3.20 implies the model is not significant relative to the noise. There is a 11.33% chance that an F-value this large could occur due to noise. P-values less than 0.0500 indicate model terms are significant. In this case there are no significant model terms. Values greater than 0.1000 indicate the model terms are not significant

Table No 5: Fit Statistics

Std. Dev.	4.58	**R^2**	0.5162
Mean	38.56	**Adjusted R^2**	0.3549
C.V. (%)	11.88	**Predicted R^2**	0.0471
		Adeq Precision	5.0326

The Predicted R^2 of 0.0471 is not as close to the Adjusted R^2 of 0.3549 as one might normally expect; i.e. the difference is more than 0.2. This may indicate a large block effect or a possible problem with your model and/or data. Things to consider are model reduction, response transformation, outliers, etc. All empirical models should be tested by doing confirmation runs. Adeq Precision measures the signal to noise ratio. A ratio greater than 4 is desirable. The ratio of 5.033 indicates an adequate signal. This model can be used to navigate the design space.

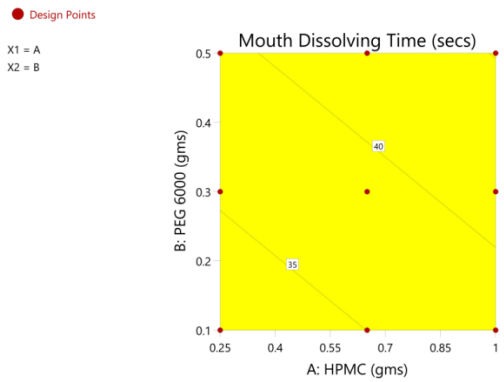


Figure3: Contour Plot of Mouth Dissolving Time

As the Concentration of PEG 6000 and HPMC increases, the mouth dissolving time of the film also increases.

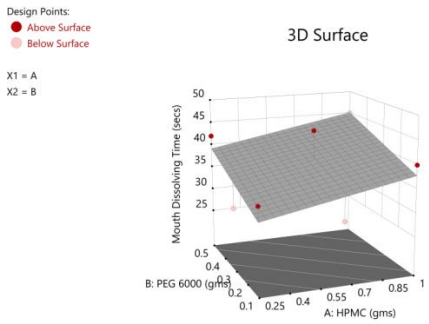


Figure: 3D Contour Plot of Mouth Dissolving Time

Evaluation of Diclofenac Sodium Fast Dissolving Film:
Physical Appearance:

The physical appearance was evaluated visually. The prepared films were clear in appearance, flexible and smooth. The results are mentioned in table 6.3. The F2 Film was formed very nicely, whereas Film F1, F3, F5, F6, and F9 were formed and F4, F7 and F8 films were not formed. Hence, 0.625 gm HPMC and 0.1 gm PEG 6000 were Suitable for the forming a very nice film.

Figure5: F2 film of Diclofenac Sodium

Table No 7: Physical appearance of Fast Dissolving Film

Batch No.	Physical Appearance
F1	Film is formed
F2	A very nice film is formed
F3	Film is formed
F4	Brittle, film is not formed
F5	Film is formed
F6	Film is formed
F7	Brittle, film is not formed
F8	Brittle, film is not formed
F9	Film is formed

Thickness:

The Thickness of the Film was measured at 5 different points of the film using a screw gauge. The Results of Film thickness are given in Table 3.4 The average film thickness was ranging between 0.010

to 0.020 mm. Hence, very thin film was able to form. For Film F7, least thickness was observed i.e. of 0.012 mm.

Figure 4: Strips of Film of Diclofenac Sodium

Table No 6: Results of Film Thickness

Film	Thickness (mm)
F1	0.016
F2	0.014
F3	0.015
F4	0.013
F5	0.014
F6	0.015
F7	0.012
F8	0.013
F9	0.015

Weight Variation test:

The Weight variation test was performed to evaluate the uniformity between the films and reproducibility of the employed method. The results of film weight variation are mentioned in Table 6.5. The Maximum weight variation obtained was 0.03 gm for batch F5. It can be seen from the results that not much weight variation was observed.

Table No 8: Results of Film Weight variation

Film	Weight variation (gm)
F1	0.02
F2	0.01
F3	0.01
F4	0.01
F5	0.03
F6	0.01
F7	0.01
F8	0.01
F9	0.02

Surface PH:

The Surface pH results are mentioned in Table 3.6. The ideal Surface pH is supposed to range between 6-7 so that it does not cause irritation to the patient. It can be seen that the surface pH for all the formulations ranging in the ideal pH range which justifies that it can consumed safely.

Table No9: Results of Surface pH

Film	Surface pH
F1	6.8
F2	6.2
F3	6.3
F4	6.3
F5	6.4
F6	6.4
F7	6.5
F8	6.3
F9	6.6

Folding Endurance test:

The Folding endurance test is performed to check the durability of the formed film. The results of the folding endurance test are given in Table 6.7. The maximum folding endurance found was 132 times for F6 batch and all the formulations showed the folding endurance above 100 times which indicates that the prepared films are durable.

Table No 11: Results of Folding Endurance Test

Film	No of folds (times)
F1	120
F2	125
F3	130
F4	118
F5	130
F6	132
F7	128
F8	130
F9	132

Percentage Moisture loss: The Results of Percent Moisture loss is given in Table 6.8. From the table it can be observed all the batches exhibited very less moisture loss which indicates that it contained very less moisture and are stable upon storage.

Table No 10: Results of % Moisture Loss

Film	% Moisture Loss
F1	0.005
F2	0.003
F3	0.003
F4	0.002

F5	0.003
F6	0.005
F7	0.002
F8	0.002
F9	0.004

Disintegration time:

The Disintegration time was performed to evaluate time taken by film to disintegrate in in-vitro conditions. The results of Disintegration time are given in Table 6.9. The average time taken by films to disintegrate was 30-35 seconds which is good for fast dissolving films and hence can be comparable to that of those to in-vivo time required to disintegrate.

Table No12: Results of Disintegration time

Film	Disintegration time (seconds)
F1	35
F2	30
F3	40
F4	30
F5	45
F6	40
F7	42
F8	40
F9	45

In vitro Wetting time:

The In vitro wetting time results are mentioned in Table 3.10. The wetting time for all the formulation was between 25-40 seconds which indicates that the moisture is getting absorb rapidly which would help the film to disintegrate fast and give faster onset of action.

Table No13: Results of In vitro Wetting Time

Film	Wetting time (sec)
F1	30
F2	35
F3	28
F4	30
F5	32
F6	34
F7	30
F8	35
F9	40

Mouth Dissolving Time:

The mouth dissolving time was evaluated by using phosphate buffer pH 6.8 as artificial saliva. The Time taken by the film to dissolve is mentioned in Table 3.11. The Mouth dissolving time was also found to be faster. Hence, which can be concluded that the faster the mouth dissolving time, the faster will be the drug absorption and faster will be the therapeutic onset of action.

Table No 15: Results of Mouth Dissolving Time

Film	Mouth Dissolving Time(sec)
F1	35
F2	30
F3	40
F4	30
F5	45
F6	40
F7	42
F8	40
F9	45

Drug Content Uniformity:

The Average drug content of the film was evaluated to check the amount of drug incorporated in to the formulation. The results of Drug Content is given in Table 3.12. In all the formulations, the Diclofenac sodium was found to be between 98-101%.

Figure: **F2 film of Diclofenac Sodium**Figure: **F1 to F9 Batches of film of DiclofenacSodium**

TableNo14: Results of Drug Content Uniformity

Film	Drug Content Uniformity (%)
F1	98.93
F2	99.47
F3	99.29
F4	100.22
F5	99.49
F6	100.34
F7	98.56
F8	98.99

F9	99.18

SUMMARY & CONCLUSION:

Summary: Tablets and capsules can be difficult for paediatrics and elderly patients. This can be a major problem of patient acceptability. So to overcome this problem, fast dissolving film of Diclofenac sodium were prepared.The Fast Dissolving Film of Diclofenac sodium was prepared by using solvent casting method. HPMC and PEG 6000 were used as polymers to prepare the films. The polymeric solution of Diclofenac sodium was prepared by dissolving HPMC, PEG 6000 and Diclofenac sodium in water and the solution was poured into the petri plate and the solution was allowed to stand at room temperature for 24 hours and the solvent was allowed to evaporate.

The prepared films were evaluated for various parameters like Physical appearance, Thickness, Weight variation, Surface pH, Folding endurance, Percentage moisture loss, Disintegration time, In vitro wetting time, Mouth Dissolving time and Drug content uniformity.

The Physical appearances of all the films were clear in appearance, flexible and smooth. The thickness of the films were between 0.012 to 0.016 mm. The weight variation was also found to be less than 0.03 gm for all the preparations. The surface pH was also between 6-7. The folding endurance also showed that all the formulations are durable. The percentage moisture loss was also less than 0.01%. Disintegration time, In-vitro wetting time and mouth dissolving time were all less than 60 seconds.The Drug Content uniformity also showed that the Diclofenac sodium incorporated into the films was between 98-101%.

Conclusion: An attempt was made to formulate and evaluate Fast dissolving film of Diclofenac sodium. The Formulation was successfully prepared by solvent casting method and the prepared films were evaluated for various physicochemical parameters like Physical appearance, Thickness, Weight variation, Surface pH, Folding endurance, Percentage moisture loss, Disintegration time, In vitro wetting time, Mouth Dissolving time and Drug content uniformity. From the evaluations, it was found that F2 batch was ideal fast dissolving film as the film was nicely formed. Therefore, it can be concluded that the Fast Dissolving films can be a potential candidate to delivery Diclofenac sodium.

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