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FORMULATION AND EVALUATION OF ORO DISPERSIBLE FILMS OF ETORICOXIB USING POLYVINYL ALCOHOL

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ABSTRACT:
The goal of the current study is to develop orodispersible films containing etoricoxib to improve therapeutic efficacy by improving patient compliance and convenience for both younger and older patients. Varied batches of Oro-dispersible films (ODF) of etoricoxib were produced by the solvent casting process using varied quantities of PVA, sodium starch glycolate, sodium, saccharine, vanillin, and purified water. The films were then assessed for appearance, weight variation, thickness, folding endurance, drug content, disintegration time, and in vitro drug release. The optimized formulation A5 exhibited acceptable folding endurance (more than 25), least disintegration time (50seconds), highest drug content (55.18 mg) and highest drug release (103.6±0.12 %) in 10minutes. The study concludes that formulation A4 of Oro Dispersible Films for sublingual delivery of etrocoxibe may be an optimal formulation. The developed formulation can be a unique dosage form to improve drug release, beginning of action, and patient compliance. The optimized formulation yields satisfactory results.

KEYWORDS: Oro Dispersible Films, Arthritis, Etrocoxibe, PVA.

1. INTRODUCTION:

The oral route is the most widely accepted route of drug administration due to the numerous advantages offered over other routes.[1] This route is non-invasive, easy to carry, and over-dosage can be easily managed. The inability to take tablet, pills and capsules, particularly in child patients and older individuals, is a significant drawback. The disadvantage of swallowing difficulties and choking anxiety associated with tablets, capsules, and oral disintegrating tablets, respectively, has been lessened with the introduction of oral dissolving films, particularly for younger and older patients. The films are stamp-sized, incredibly thin compositions that include excipients and active substances.[2]

Oro Dispersible Films (ODF) are the most new form of solid oral dosage form due to more flexibility and comfortODF increases the medication's effectiveness by solubilizing in the mouth cavity in less than a minute following contact with saliva. The oral film that makes up the delivery system is extremely thin. When these films are placed under the tongue, the drug is instantly hydrated and released. Subsequently, it dissolves and melts, allowing the drug to be absorbed through the oromucosa. Due to the oral mucosa's 4-1000-fold greater permeability than the skin's, the increased blood flow will increase the drug's bioavailability. The benefits of oral disposable

films over the other oral dosage forms is it provides improved oral bioavailability bypassing the first pass effect. [3, 4]

Arthritis is a medical condition in which joint inflammations commonly referred as "Arthritis "[5] Etoricoxib belongs to the NSAID class of drug, Etoricoxib, a selective COX-2 inhibitor in the NSAID class of medication, is used to treat mild post-surgical dental pain in the short term and to reduce inflammation and pain associated with different types of arthritis. Using varying concentrations of PVA and together with sodium starch glycolate, PEG 400, sodium saccharine, vanillin, and purified water, several batches of Oro Dispersible Films of Etoricoxibwere produced[6].

2. MATERIALS AND METHODS:

2.1Materials:

Etoricoxib obtained from Yarrow chem, PVA, and Maltodextrine, Sodium Starch Glycolate, Saccharine, Tartrazines, Disodium hydrogen phosphate and Potassium dihydrogen phosphate from Kailash Institute of Pharmacy and Management GIDA Gorakhpur.

2.2 Methods:

Formulation of drug loaded Oro- Dispersible Films:

The technique involved in the preparation of Oro dispersible film was solvent casting method in which aqueous solution I (polymer &glycerin) and aqueous solution II (drug, Mannitol, SSG, and Tartrazines) was prepared in specific proportion in distilled water. Both solution I & II were mixed slowly & stir for 1 hour & kept for 1 hour to remove all air bubbles. Then the mixture solution was poured into petridish & it was dried in oven at 40-50^{0}C for 7- 8 hours (fig-1) then film was removed from petridish and cut according to size (square film: 1cm length, 1cm width). Composition of ODF shown in table-1.

Table 1. Composition of ODFs using PVA

Name of Ingredients	Quantity (in mg)					
	A1	A2	A3	A4	A5	A6
PVA	10	15	20	10	15	20
Mannitol	6	6	6	6	6	6
Glycerin	4	4	4	6	6	6

3. Evaluation of prepared Oro- Dispersible Films:

All the Oro Dispersible Films of Etoricoxib were subjected to following quality control tests.

3.1. Physical appearance and Surface Texture[7]

The films were subjected for determine the physical appearance and texture by visual inspection.

3.2. Weight Variation [8,9]

Ten films of 1x1 cm^{2}were individually weighed using digital weighing balance. The standard deviations of weight variation were calculated.

3.3. Thickness Uniformity [8,10]

The thicknesses of the films at three different points were measured by using screw gauge.

3.4. Folding endurance [8,11-13]

The film was subjected to folding endurance by folding the film at the same place repeatedly several times until to break or visible crack was observed.

3.5. Surface pH of Film [7,9]

The film was kept in phosphate buffer pH 6.8 for a period of 2 h at room temperature. The pH was measured by using pH meter after being equilibrated for 1 minute.

3.6. Drug Content: - [14-15]

A film of size 1 cm^2 was cut and put 10 ml of volumetric flask which containing solvent. This was then shaken in a mechanical shaker for 2hrto get a homogeneous solution and filtered. The drug was determined spectroscopically at 233 nm.

3.7. Tensile Strength: [16, 17]

Tensile strength of films was determined using an apparatus fabricated in laboratory. A small film strip ($2cm^2$) was cut and fixed to assembly. The weight required to break the film was noted and simultaneously film elongation was measured with the help of pointer mounted on the assembly.

$$\% \text{ Tensile Strength} = \frac{\text{Load at Failur}}{\text{Film Thickness}} \times \text{Film Width} \times 100$$

38. Percentage elongation:[18-19]

Determined by noting the distance travelled by pointer before break of the film on the graph paper.

% elongation = increase in length/original length X 100.

3.9. Disintegration Time [14-16]

Determined manually by dipping the film in 10 ml of water in beaker with gently shaking when film was dissolved, time was noted.

3.10. *In-vitro* dissolution studies[17-23]

The IP Drug Dissolution Apparatus I (Paddle type) was used to measure the in vitro release. To keep the oral strip (1 × 1 cm2) from floating throughout the test, it was adhered to rectangular glass plates. It was then put at the bottom of a dissolving vessel that was filled with 900 milliliters of pH 6.8 phosphate buffer, heated to 370 degrees Celsius, and rotated at 50 revolutions per minute. A five milliliters sample was taken every one to ten minutes, and the same volume was replenished with fresh buffer solution that was maintained at 37 degrees Celsius. Using a double beam UV/visible spectrophotometer (Shimazdu 1800), the samples were filtered and examined at 233 nm. The drug content was determined using an equation derived from the standard calibration curve of Etrocoxibe.

4. Result and Discussion:

4.1 Formulation of Oro- Dispersible Films:

The formulated Oro Dispersible Films of Etoricoxib are uniform shown in figure 1.

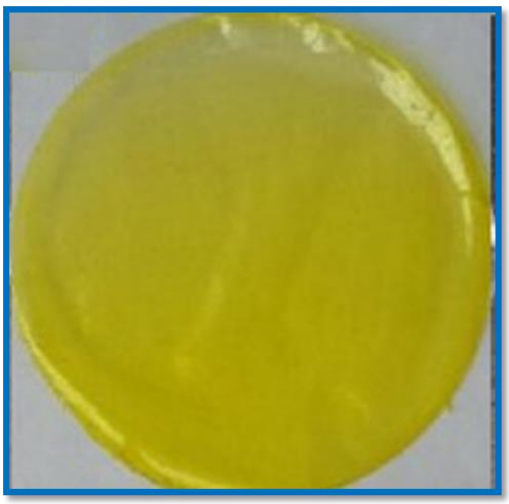

Fig 1. Formulated Oro Dispersible Films of Etrocoxibe

5. Evaluation of Mouth Dissolving Films:

5.1. Physical appearance and Surface Texture:

All films are clear, transparent, smooth and free from foreign materials and air bubbles with odor of vanilla.

5.2. Weight variation:

The percentage weight deviation of films between **106±0.671** was shown in table 2. The A4 formulation shows less weight variation.

5.3. Thickness uniformity:

Thickness of films was shown in table 2. The thickness of films is 1.3**±0.054**

5.4. Folding Endurance:

The folding endurance of films between more than 25 times was shown in table 2. It was observed that increase the folding endurance of films when increase in concentration of the polymer.

5.5. Disintegration:

Disintegration of Oro Dispersible Films was shown in table 2. It was observed that increase the disintegration time of films, when increase in concentration of the polymer. All the formulation shows disintegration time less than 110 seconds. The A4 formulation shows least disintegration time was 50 seconds.

5.6. Drug content:

The drug content in various batches of film was shown in table 2. The A4 formulation shows highest amount of drug content was 55.18 mg compared to other formulations.

5.7. *In-vitro* drug release:

The *in-vitro* dissolution in various batches of film shown in table 3. All the formulation shows drug release range from 103 %. The A4 formulation shows better drug release was 102.6±0.22 % at 10 minutes.

Table 2. Evaluation of ODFs using PVA

batches	Thickness ± SD*(mm)	Wt. Variation ±SD* (mg)	Tensile Strength ±SD*(Kg/mm^2)	Folding endurance (No. of folds)	Dissolving Time (Sec)	% Elongation ±SD*	Drug Content (mg)
A1	0.81+0.0083	112±0.517	1.37±0.017	>25	50	232±1.152	54.77
A2	0.92+0.0070	114±1.52	2.26±0.005	>25	55	280±1.124	54.77
A3	1.1±0.010	107±0.517	2.4±0.034	>25	59	235.3±1.152	57.28
A4	1.3±0.054	106±0.671	2.29±0.154	> 25	50	298.1±1.152	55.18
A5	0.8±0.005	115±1.52	2.4±0.029	>25	51	257±1.541	58.89
A6	0.93±0.005	113±0.571	2.18±0.049	>25	78	303±2.882	54.79

Data are presented as mean ± SD (n = 3).

Table 3. *In-vitro* drug release of ODFs using PVA

Time (min)	Cumulative Release (%)					
	A1	A2	A3	A4	A5	A6
0	0	0	0	0	0	0
1	82.6047	85.3953	89.4419	90.9767	48.8372	66.4186
2	91.755	90.3907	93.8186	98.0558	90.124	84.1798
3	93.6016	93.6171	97.6837	99.9674	94.7473	93.3395
4	93.7829	95.1938	99.9023	102.395	97.1783	94.4977
5	94.9318	97.9627	103.07	102.986	98.2295	95.3783
10	95.524	98.555	105.684	103.633	97.8853	95.9783

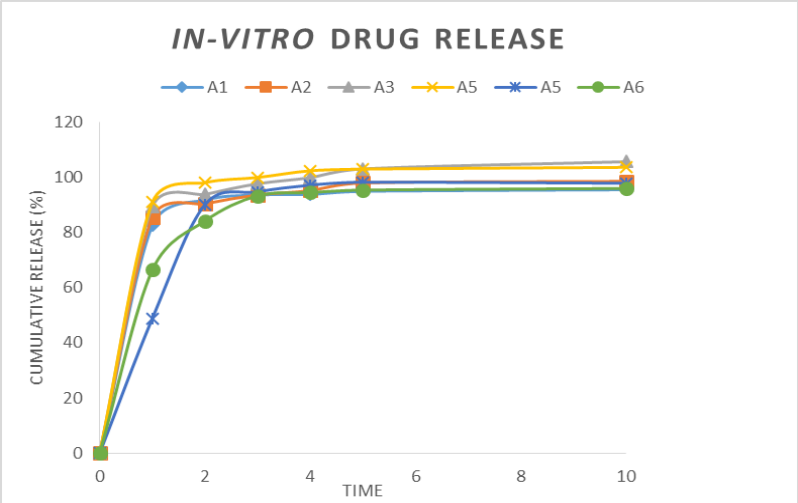

Fig - *In-vitro* drug release of ODFs using PVA

6. Conclusion:

According to the current investigation, all six of the Oro Dispersible Films that were created demonstrated acceptable film parameters. We may conclude that the solvent casting approach can be used to make an Oro dissolving film containing etoricoxib. Each formulation has the ideal thickness and weight variation, and it demonstrates the necessary folding endurance and disintegration duration of 52 seconds. In contrast to other formulations that incorporate polymer, formulation A4 exhibits the lowest disintegration time (50 seconds), the largest drug content (55.18 mg), and the maximum drug release (10 minutes) of approximately 103.6 %.

7. Acknowledgement:

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8. Conflict Of Interest:

Authors are declared no conflict of interest.

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