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(Original Research Article)

Development Formulation and Evaluation of Buccal Patch of Ondansetron and Aceclofenac for Treatment of Headache Induce Vomiting

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Abstract

Migraine and other headache disorders are often accompanied by gastrointestinal symptoms such as nausea and vomiting, which can hinder the efficacy of orally administered medications due to delayed gastric emptying and decreased absorption. The current study aims to develop and evaluate a novel fast-dissolving mucoadhesive buccal film incorporating ondansetron hydrochloride, an antiemetic, and aceclofenac, a non-steroidal anti-inflammatory drug (NSAID), to achieve a dual therapeutic effect. The buccal route was selected to circumvent first-pass metabolism and enable rapid drug absorption through the oral mucosa.

Buccal films were formulated using the solvent casting technique, utilizing hydrophilic polymers such as Hydroxypropyl methylcellulose (HPMC E15) and Polyvinyl alcohol (PVA), and plasticized with glycerin to impart flexibility. A series of formulations were developed with varying polymer ratios, and the films were characterized for physicochemical properties, mechanical strength, surface pH, disintegration time, drug content uniformity, in vitro drug release, and stability over accelerated conditions.

The optimized formulation (F5) exhibited excellent folding endurance, rapid disintegration (~25 sec), and a cumulative drug release of more than 90% for both drugs within 10 minutes. FTIR and DSC studies confirmed the compatibility of active drugs with excipients, while SEM imaging revealed uniform drug dispersion. The results suggest that the developed dual-drug buccal film holds promise for the prompt management of headache accompanied by vomiting, especially in conditions where oral ingestion is compromised.

Keywords: Buccal drug delivery, Ondansetron hydrochloride, Aceclofenac, Headache-induced emesis, Solvent casting, Mucoadhesive film, Rapid onset.

INTRODUCTION

Headache is a very common condition where pain is felt in the head, face, or neck. The pain may be sharp, dull, or throbbing. Although most headaches are not serious, they can significantly affect daily life.

Various Types of Headaches are

Migraine: Severe pain usually on one side of the head, often with nausea, vomiting, and sensitivity to light and sound.

Tension Headache: Dull pain on both sides, often caused by stress or muscle strain.

Cluster Headache: Intense pain around one eye, occurring in repeated episodes.

Causes: Stress, dehydration, infections, poor sleep, and certain foods or medications.

Some headaches may be secondary to underlying health issues like sinus infections or trauma.

Vomiting is the forceful expulsion of stomach contents. It's often caused by infections, motion sickness, pregnancy, or medications. Common causes are Nausea, abdominal pain, dizziness, dry mouth, and reduced urination.

Buccal films are thin, flexible drug delivery systems placed on the inner cheek. They release drugs directly into the bloodstream, bypassing the digestive system.

Ondansetron is a serotonin 5-HT_3 receptor antagonist used to prevent nausea and vomiting. It works by blocking serotonin in the brain and gut. Aceclofenac is an NSAID used for pain and inflammation. It works by inhibiting COX enzymes and reducing prostaglandin synthesis.

Material and methods

Materials: Ondansetron HCl was received as a gift sample from Shodhana Laboratories Aceclofenac Emcure Pharmaceuticals along with a certificate of analysis; it was analyzed by the methods recommended by IP. The procured sample was validated by performing the following tests, such as colour, odour, pH, melting point, solubility, residue on ignition %, and % purity. All the excipients used in this formulation were of analytical grade.

Table 1: Formulation Table

Ingredients (mg)	FL1	FL2	FL3	FL4	FL5	FL6	FL7	FL8	FL9
Ondansetron	8	8	8	8	8	8	8	8	8
Aceclofenec	100	100	100	100	100	100	100	100	100
Sodium Alginate	100	125	150	-	-	-	-	-	-
Chitosan	-	-	-	75	100	125	-	-	-
HPMC(Hydroxypropyl methylcellulose)	-	-	-	-	-	-	30	40	50
Sodium Starch Glycolate	50	75	100	125	150	-	-	-	-
Starch	-	-	-	-	-	20	30	40	50
Phenoxyethanol	20	20	20	20	20	20	20	20	20
Honey (ML)	2	2	2	2	2	2	2	2	2
PVA (polyvinyal alcohol)	10	10	10	10	10	10	10	10	10
Propylen glycol	100	100	100	100	100	100	100	100	100
Brilliant Blue FCF	5	5	5	5	5	5	5	5	5
Strawberry (ML)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Distilled Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
TOTAL (mg)	395	445	495	445	495	390	305	325	345

Methods: The buccal films were prepared by the solvent casting method:

Polymer Dissolution: The chosen polymer (Sodium Alginate, Chitosan, or HPMC) was dissolved in a fraction of distilled water under stirring. For chitosan, it was dissolved in 1% acetic acid initially and then mixed with the aqueous phase.

Incorporation of Drug and Excipients:

Ondansetron and Aceclofenac were dissolved/dispersed in the solution of the polymer. The remaining excipients (super-disintegrate, PVA, honey, phenoxyethanol, propylene glycol, flavour, and colorant) were added progressively under stirring to have homogeneity.

Casting and Drying:

The resulting mixture was poured onto a fresh Petri dish or flat glass mold. Films were dried at room temperature for 24–48 hours in a dust-free area.

Cutting and Storage:

Following drying, films were gently peeled off and cut into equal sizes (e.g., 2 × 2 cm) with the desired drug dose. Films were stored in sealed containers at room temperature for further assessment

Result and Discussion

Physical Characterization of Buccal Films

Nine formulations (FL1–FL9) were successfully preparedusing varying polymer compositions. All films were smooth, flexible, and uniform in appearance. The differences among the nine formulations revealed insights into the impact of various polymers on film properties.

Disintegration Time in 0.1 N HCl: All formulations demonstrated rapid disintegration, ideal for buccal delivery, and the formulation FL6 having minimum disintegration time.

Drug Content (%): Drug content was within acceptable pharmacopeia limits (80–120%), Indicating uniform distribution. Drug content analysis was performed using UV-spectrophotometric methods and revealed that all formulations contained between 80.1% and 86.63% of the expected drug load. In all formulation the FL6 Having the maximum drug content.

In Vitro Drug Release (Zero Order Kinetics):

All films followed zero-order release kinetics, indicating a controlled and sustained release of drug content. Maximum drug release ranged from 84–86% over 60 minutes.

The in vitro drug release profile of the films was evaluated using a dissolution testing apparatus with 0.1 N HCl as the medium. The results showed that all formulations followed zero-order release kinetics, meaning the rate of drug release was constant over time and not dependent on drug concentration. This characteristic is particularly desirable in buccal drug delivery systems where sustained and predictable drug levels are necessary for consistent therapeutic effects. Maximum drug release for most formulations exceeded 80% within 60 minutes, with the highest being 86.31%, observed in formulation FL6.

Evaluation of buccal Film of ondansetron and Aceclofenac: Physical appearance and surface texture of the patch: This parameter was checked simply with a visual inspection of films and an evaluation of texture by feel or touch.

Weight uniformity of films: Nine films of the size 4cm^2 diameter were weighed individually using digital balance and the average weights were calculated. Now average weight is use as a standard weight and in all of these F1 to F9 formulation near to standard weight is having good uniformity.

The thickness of films: The thickness of the films was measured using a screw gauge with a least count of 0.01mm at different spots of the films.

Folding endurance of films: The flexibility of films can be measured quantitatively in terms of what is

known as folding endurance. The folding endurance of the films was determined by repeatedly folding a small strip of the films (approximately 2x2 cm) at the same place till it broke. The number of times films could be folded at the same place, without breaking gives the value of folding endurance.

Surface pH of films: Surface pH was determined by the films allowed in contact with 1 ml of distilled water. The surface pH was noted by bringing a combined glass electrode or pH paper near the surface of the films and allowing equilibration for 1 min.

Table 2: Physical Characteristics of Formulation

Formulation Code	Color	Transparency	Surface	Surface PH	Folding Endurance	Weight (mg)
FL1	Light Blue	Semi -transparent	Smooth	6.82 ± 0.01	>250	167.00 ± 1.00
FL2	Light Blue	Semi -transparent	Smooth	6.80 ± 0.01	>250	170.00 ± 1.00
FL3	Light Blue	Semi -transparent	Smooth	6.85 ± 0.01	>250	171.00 ± 1.00
FL4	Light Blue	Slightly Opaque	Smooth	6.79 ± 0.01	>250	169.00 ± 1.00
FL5	Light Blue	Slightly Opaque	Smooth	6.81 ± 0.01	>250	169.00 ± 1.00
FL5	Light Blue	Slightly Opaque	Smooth	6.82 ± 0.01	>250	168.00 ± 1.00
FL6	Light Blue	Light transparent	Smooth	6.81 ± 0.01	>250	162.00 ± 1.00
FL7	Light Blue	Light transparent	Smooth	6.80 ± 0.01	>250	160.00 ± 1.00
FL8	Light Blue	Light transparent	Smooth	6.82 ± 0.01	>250	165.00 ± 1.00
FL9	Light Blue	Light transparent	Smooth	6.84 ± 0.01	>250	164.00 ± 1.00

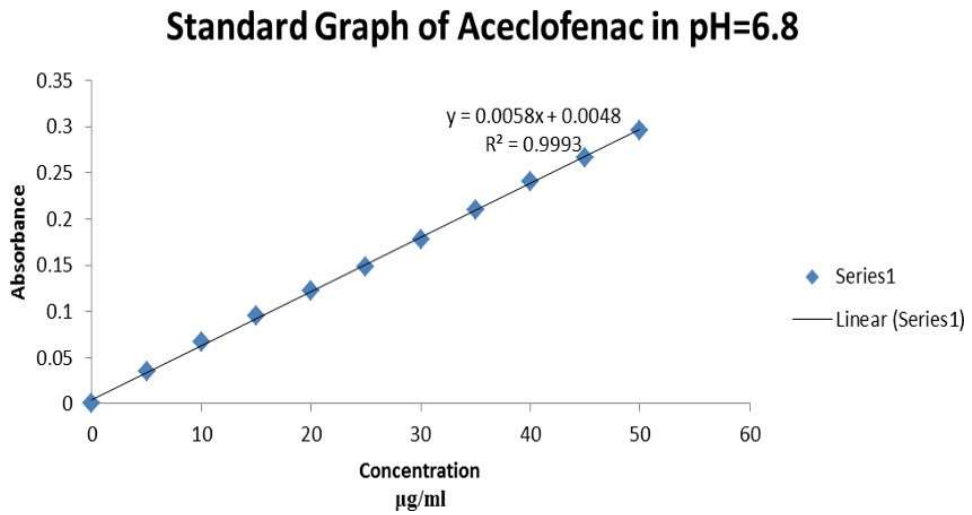

Figure 1: Standard curve of Aceclefenac

In vitro disintegration time of films: The disintegration test was performed in the USP disintegration time testing apparatus. 0.1N HCl solution was used as a medium.

Table 2: Disintegration Time

Formulation Code	FL1	FL2	FL3	FL4	FL5	FL6	FL7	FL8	FL9
Time (Sec.)	50	49	44	45	48	37	42	46	41

Drug content uniformity study of films: The films were tested for drug content uniformity by a UV-Spectrophotometric method. Films of 2 cm diameter were cut from three different places from the casted films. Each patch was placed in a 100 ml volumetric flask and dissolved in 0.1N HCl solution and 0.2 ml is taken and diluted with water up to 10 ml.

In-vitro Dissolution Study: In vitro dissolution of aceclofenac and Ondansetron Oral disintegrating thin films was studied in USP XXIV dissolution test apparatus 900ml 0.1N HCL solution was used as dissolution medium. The stirrer was adjusted to rotate at 50rpm. The temperature of the dissolution medium was maintained at 37±0.5ºC throughout the experiment. One film was used in each test. Samples of dissolution medium (5ml) were withdrawn utilizing a syringe fitted with a pre-filter at known intervals of time and analyzed for drug release by measuring the absorbance at 310 nm.

Drug content %: Drug content refers to the amount and identity of the active ingredient(s) in a pharmaceutical product or drug formulation. Drug Content (%)= Actual amount of drug in Film Divided by theoretical amount of drug *100

Table 3: Zero Order Release Rate Kinetics

Time(min.)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	27.397	28.326	29.588	28.76	28.578	27.76	29.478	25.76	28.432
10	42.388	41.134	40.147	41.52	40.578	41.52	44.147	42.52	40.592
15	53.895	53.147	52.453	51.378	50.895	50.378	49.453	50.378	50.294
30	69.785	68.441	68.365	65.486	70.785	66.486	70.365	65.486	65.376
45	77.765	77.431	79.358	77.269	77.765	75.269	77.358	77.269	74.396
60	82.420	80.100	83.750	85.140	83.550	86.630	85.660	84.360	81.960

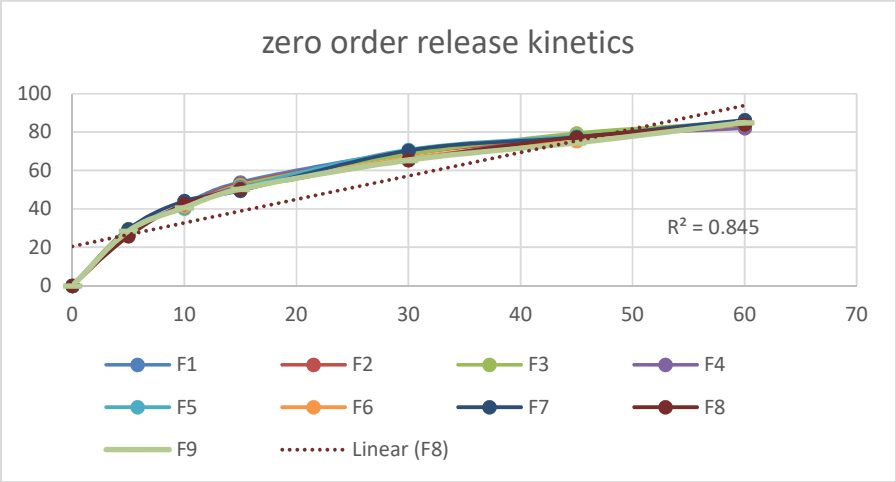

Figure 2: Graph Zero Order Release

Table 4: First Order Release Rate Kinetics

Time (Min.)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	2	2	2	2	2	2	2	2	2
5	1.851	1.856	1.842	1.852	1.863	1.857	1.847	1.859	1.863
10	1.788	1.731	1.731	1.781	1.673	1.781	1.777	1.786	1.768
15	1.673	1.651	1.677	1.695	1.69	1.695	1.689	1.695	1.695
30	1.48	1.525	1.5	1.562	1.572	1.562	1.568	1.555	1.568
45	1.327	1.407	1.314	1.427	1.462	1.427	1.427	1.429	1.435
60	1.176	1.248	1.274	1.184	1.246	1.287	1.281	1.293	1.275

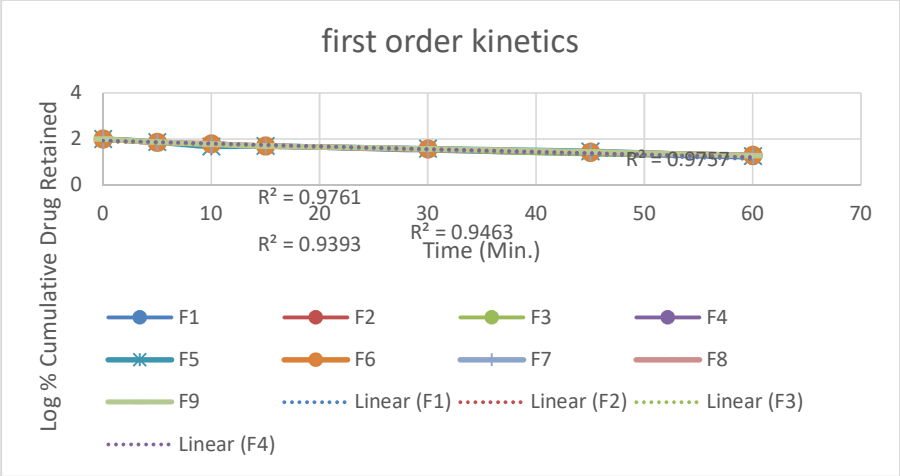

Figure 3: Graph Zero Order Release

CONCLUSION

The present study successfully developed and evaluated buccal films of ondansetron and aceclofenac for the management of headache-induced vomiting. The films demonstrated: Excellent flexibility (folding endurance >250), Ideal pH (6.79–6.85) for buccal mucosa Rapid disintegration (37–50 seconds) High drug content (80–86%) Sustained drug release following zero-order kinetics.Formulations FL6 and FL7 showed the best overall performance, combining rapid disintegration, good mechanical strength, and consistent drug release.

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