International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 1896-1904 www.ijprajournal.com ISSN: 2456-4494

Design and Assessment of Buccal Tablets of Aceclofenac Using Synthetic and Natural Polymer

Dr. V. Kamalakkannan
Dr. B. Sangameswaran, B. Madhava praveen, B. Kaviya, G. Madhan, M. Logeshwaran, SSM College of Pharmacy, Jambai, Erode district, Tamil Nadu

Date of Submission: 04-12-2023 Date of Acceptance: 17-12-2023

ABSTRACT
This work was aimed to formulate and characterize mucoadhesive buccal tablets of Aceclofenac, utilizing different proportions of two synthetic polymers, Carbopol 934 and Hydroxypropyl methylcellulose and two natural polymers, Tragacanth and Soluble Starch. An examination of Fourier Transform Infrared Spectroscopy revealed no indication of drug excipient interaction. Six batches of Bucco adhesive Aceclofenac were prepared by the direct compression method. The compressed tablets were then evaluated for physicochemical parameters such as hardness, thickness, weight variation, drug content, friability, swelling index and surface pH. In vitro dissolution test was conducted for 8 hours, using the rotating paddle method in phosphate buffer of pH 6.8 maintained at 370 c. Physiochemical parameters like weight variation, hardness, friability, diameter, thickness, drug content, surface pH, swelling index were within the acceptable limit. The dissolution profile of all the batches varied greatly, with a maximum release of to a minimum release of. Among them, only batch 1 ensured sustained and effective drug release with appropriate swelling index. Thus, the findings indicated that it is possible to create Aceclofenac pills that are buccal mucoadhesive. Moreover, the behavior of the polymers utilized determines the tablet's properties in addition to its concentration.

KEYWORDS: Aceclofenac, Buccal tablets, Mucoadhesion, Sustained release, Swelling index.

I. INTRODUCTION

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms.[1]

It also has some major disadvantages such as the first-pass effect, gastrointestinal enzymatic degradation, and slow onset of action.[2] To overcome these disadvantages, mucoadhesive drug delivery and sublingual drug delivery could be better alternatives.[3]

Various mucoadhesive polymers (natural, semi-synthetic, and synthetic) used in this delivery system become adhesive on hydration, therefore can be used for targeting a drug to a particular region of the body. Initially, when the mucoadhesive product is in contact with the mucosal membrane, it swells and spreads, initializing deep contact with the mucosal layer and then mucoadhesive materials (polymers) are activated by the presence of moisture and drug releases slowly.[4,5]

The main objective of the study is to formulate Aceclofenac buccal tablets by using natural and synthetic polymers having acceptable mechanical properties and faster dissolution.

Strong cyclooxygenase-2 (COX-2) inhibitor, Aceclofenac is a more most recent non-steroidal anti-inflammatory drug (NSAID) with good analgesic, anti-pyretic, and anti-inflammatory properties. It is primarily used to treat rheumatoid arthritis, osteoarthritis, dental pain, and other rheumatoid disorders. It is a highly permeable derivative of aryl acetic acid that is insoluble in water. It is classified as a class II drug under the Biopharmaceutical Classification System (BCS).[6] It has a brief biological half-life of 4–4.3 hours and is heavily protein-bound. 100 mg of Aceclofenac is often taken twice or three times a day. In addition to causing several inconveniences and therapeutic fluctuations, the traditional dose form of Aceclofenac has various unfavourable side effects, including gastric ulcers, gastrointestinal bleeding, and gastrointestinal disturbances. Hence, developing sustained-release pharmaceuticals is an excellent way to decrease the frequency of doses, achieve a longer-lasting effect with better

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 1896-1904 www.ijprajournal.com ISSN: 2456-4494

bioavailability, and enhance the medication's safety and effectiveness.[7]

II. MATERIALS AND METHODS

2.1 Drug and chemicals

Aceclofenac was obtained as a gift from Gift sample of Apex formulation, Chennai**.** Carbopol 934 (CP) was purchased from Fine chemicals, Mumbai**.** . Hydroxypropyl methylcellulose (HPMC)) was purchased from Research lab fine chem industries, Mumbai. Tragacanth and soluble starch were purchased from Nice chemicals, Mumbai. Micro crystalline cellulose powder, Magnesium stearate and Talc were purchased from Lobo chemie, Mumbai.

2.2 Instruments

UV Visible Spectro photometer(UV 1800 SHIMAZU, Japan), FT-IR Spectro photometer(SHIMADZU, Japan), Digital balance(Satorious 21.00), P^H Tester(Digital P^H Meter), Dissolution Tester(Singhla Apparatus), Hardness Tester(Monsanto hardness tester), Thickness tester(Mitutoyo vernier caliper), Friability Tester(Roche Friabilator).

III. PRE-FORMULATION STUDIES

3.1. Determination of Calibration Curve

a) Determination of λmax

Weighed 10 mg of Aceclofenac and dissolved in 10 ml of pH 6.8 phosphate buffer solution (1000µg/ml). From this solution 1ml was taken and diluted to 10ml with PBS to get a solution containing 100µg/ml. From this 1ml was diluted to 10ml to get working standard solutions of 10µg/ml. The resultant solution is scanned in the range of 200-400 nm by ultra violet visible spectrophotometer to get absorption maxima (λmax).

b) Preparation of Calibration curve

Weighed 10 mg of Aceclofenac and dissolved in 10 ml of pH 6.8 phosphate buffer solution (1000µg/ml). From this solution 0.5 ml, 1ml, 2ml, 3ml, 4 ml was taken and diluted up to 100ml using pH 6.8 phosphate buffer solution to obtain a working standard solution of 5- 40 µg/ml. The prepared concentrations were analysed in UV-Visible spectroscopy at 273 nm. A standard curve is plotted using concentration on X – axis and the absorbance obtained on Y - axis.[8]

3.2. COMPATABILITY STUDIES

a) Infrared spectroscopic studies

Infrared spectrum of Aceclofenac, Carbopol 934, Hydroxy propyl methyl cellulose, Sodium hydroxy propyl methyl cellulose and its physical mixture are obtained using infrared spectrophotometer (FT-IR 8400s Shimadzu, Japan). Samples are prepared using KBr disc method and spectra are recorded over the range 400-4000 per cm. Spectra are analyzed for drug-excipient interaction.[9]

3.3. PREFORMULATION STUDIES[10]

a) Organoleptic properties

Organoleptic properties of the drug sample were studied by visual inspection.

b) Melting point determination

Melting point of drug sample was determined by using melting point apparatus. A few quantities of drug sample were taken and placed in a thin-walled capillary tube; the tube was approximately 10-12 cm in length with 1mm in diameter and closed at one end. The capillary which contains sample was placed in melting point apparatus and heated and when drug sample was melted the melting point of sample powder was noted.

c) pH Determination

This was done by shaking a 1% w/v dispersion of the sample in water for 5min and the pH determination using a digital pH meter.

d) Loss on Drying

Weigh about 1.0g of sample, dry it at 105ºC for 3~4hrs.Cool for 30±5 minutes. It loses not more than 0.5% of its weight. Calculate as following formula,

Loss on Drying %= m_1-m_2/ m_1-m×100%

Where:

m_1 - the weight of weighing bottle and sample

m_2 - the weight of sample and weighing bottle after drying

m - the weight of weighing bottle dried to constant weight

e) Determination of solubility

Qualitative solubility analysis of drugs was done by dissolving 5 mg of drug in 5 ml of distilled water and different solvents such as HCl (0.1N), Saline phosphate buffer (pH 7.4), Phosphate buffer(pH 6.8), ethanol, acetone and chloroform were used to determine the solubility of drug.

e) Angle of repose

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane. In the method, a fixed

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 1896-1904 www.ijprajournal.com ISSN: 2456-4494

funnel method procedure is performed in triplicate and average angle of repose is calculated.

$\theta = \tan^{-1}(h/r)$ (h-height, r-radius)

f) Bulk Density

Bulk density is the ratio between given mass of powder and its bulk volume. Bulk density is carried out in triplicate. Bulk density measurements are carried by placing fixed weight of powder in graduated cylinder and volume occupied is measured and initial bulk density is calculated. It is expressed in gm/ml. Bulk density is calculated by using following formula,

Bulk Density = Mass of the powder / Bulk volume of the powder

g) True Density

True density is the ratio between given mass of powder and constant volume of powder after tapping. True density measurements are carried by cylinder is then tapped at a constant velocity till a constant volume is obtained. Then tapped density is calculated by using following formula

True density = Mass of the powder / Tapped volume of the powder

h) Carr's Index

Flowability is assessed from Carr's compatibility index (C1%). The CI is calculated from the poured (bulk density) and tapped densities. Tapped density is measured by tapping fixed weight of the sample into 100ml measuring cylinder several times using a tap density apparatus till a constant volume is obtained, where the powder is considered to reach to it most stable arrangement.

Carr's index = Tapped density – bulk density x 100 / Tapped density

The smaller the value of CI%, the superior the flow properties of the powder

i) Hausner ratio

Hausner ratio is the ratio of tapped density to bulk density. Lower the value of Hausner ratio, better is the flow property. It is calculated by the following formula

Hausner's ratio = Tapped density / Bulk density

Table 1: Formulation chart

INGREDIENTS	SF1 (mg)	SF2 (mg)	SF3 (mg)	NF1 (mg)	NF2 (mg)	NF3 (mg)
Aceclofenac	100	100	100	100	100	100
Carbopol	25	30	35	10	10	10
HPMC	60	55	50	-	-	-
Tragacanth	-	-	-	25	30	35
] Soluble starch	-	-	-	60	55	50
Magnesium stearate	5	5	5	5	5	5
MCCP	55	55	55	55	55	55
Talc	5	5	5	5	5	5
Total	250	250	250	250	250	250

3.4 Preparation of Aceclofenac Buccal Tablet

Direct compression technique was applied for the tablet compression, using varying proportions of different grades of polymer. All the powders in pure form were accurately weighed. Aceclofenac was then mixed with CP. HPMC was mixed with talc in a separate pouch. These two mixtures were then mixed for 5 min after passing through a 40-mesh sieve. MCCP 200 and magnesium stearate was added and the resultant mixtures were mixed and the blend was then compressed into tablets having an average weight of mg using single tablet punching machine. Six batches were prepared and coded as SF1, SF2 & SF3 . The details of the composition of each batch were given in Table 6. (Procedure for formulations using Synthetic polymers)

All the powders in pure form were accurately weighed. Aceclofenac was then mixed with Tragacanth. Soluble starch was mixed with talc in a separate pouch. These two mixtures were then mixed for 5 min after passing through a 40-mesh sieve. MCCP 200 and magnesium stearate was added and the resultant mixtures were mixed and the blend was then compressed into tablets having an average weight of mg using single tablet punching machine. Six batches were prepared and coded as NF1, NF2 & NF3 . The details of the composition of each batch were given in Table 1. (Procedure for formulations using Natural polymers)

3.5 POST FORMULATION STUDIES

a) Weight variation

Twenty tablets (n ¼ 20) from each batch were weighed using electronic balance and their average weight was calculated.

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 1896-1904 www.ijprajournal.com ISSN: 2456-4494

b) Hardness

Tablet requires a certain amount of hardness and resistance to friability to withstand mechanical shakes of handling in manufacturing, packing and shipping. The hardness of tablet is determined using Monsanto hardness tester. It is expressed in Kg/cm^2. Three tablets are selected from each formulation and hardness of tablet is determined. The results are expressed in average value.

c) Thickness

Thickness gauge or tester is an instrument that measures the thickness of tablets or capsules in millimetres. To measure the tablet thickness simply place the tablet in between the jaws and slide the scale jaw to press the tablet against the stationary jaw. The reading on the display is noted and it is the actual thickness of the tablet.

d) Friability test

The friability of tablets is determined using Roche Friabilator. Twenty tablets were randomly selected from each formulation and initial weight of 20 tablets are calculated, then transferred into Friabilator. The Friabilator is operated at 25 rpm for4 minutes (100 revolutions). The tablets dedusted and weighed again (final weight). The percentage friability is calculated by the following equation

Friability (%) = Initial weight – Final weight x 100 / Final weight

Compressed tablet that loses less than 0.1% to 0.8% of the tablet weight are considered acceptable.

e) Drug content determination

The total amount of drug present in the formulation is evaluated using UV spectrophotometric analysis. Approximately weighed quantity of 10mg equivalent of drug is taken from formulation which is dissolved in 10ml of methanol and the volume is made up-to 100ml with phosphate buffer 6.8. From the above solution, 10ml is taken and diluted with phosphate buffer 6.8. The absorbance of resulting solution (10 µg/ml) is measured at 257nm using spectrophotometer and the drug content is calculated from the standard curve using the formula

Drug content = Sample absorbance x 100 / Standard absorbance

f) Surface pH

The pH of three tablets (n=3) from each batch were determined. The tablets were placed in distilled water maintained at pH 6.8 and allowed to swell up to 2 hr. The surface pH of the tablet was determined by using a pH meter electrode.

g) Swelling index

From each batch, three tablets were individually weighed (W1) and placed separately in petri dishes with 5 mL phosphate buffer of pH 6.8. At the time intervals of 0.5, 1, 2, 4, and 8 h, they were taken out from the petri dish and excess water was removed by using filter paper. The swollen tablets were reweighed (W2) and the percentage of hydration was calculated for each tablet, using the equation,

Swelling index = $[(w_2-w_1) / (w_1x100)]$

h) In vitro dissolution studies

In vitro release studies of Atorvastatin fast dissolving tablets are performed by using USP type II Paddle dissolution apparatus in 900 ml of phosphate buffer pH 6.8 maintained at 37° C ± 1° C and 50 rpm. Samples (5 ml) are withdrawn at regular intervals of 10 minutes for 1hr and the same volume of fresh dissolution medium is replaced after every withdrawal. The withdrawn samples are analysed by UV- visible spectrophotometer (Shimadzu UV-1700 pharma spec, Japan) at 276nm(λmax). The studies are done in triplicate.[8]

IV. RESULTS AND DISCUSSION

4.1 Determination of Calibration Curve

a) Determination of λmax

The absorption maximum (λmax) of the Aceclofenac was estimated by scanning the drug solution (10 µg/ml) between 200 – 400 nm regions on UV spectrophotometer. The obtained spectrum showed that the absorption maximum (λmax) was 276 nm in pH 6.8 phosphate buffer which was shown in fig.1.

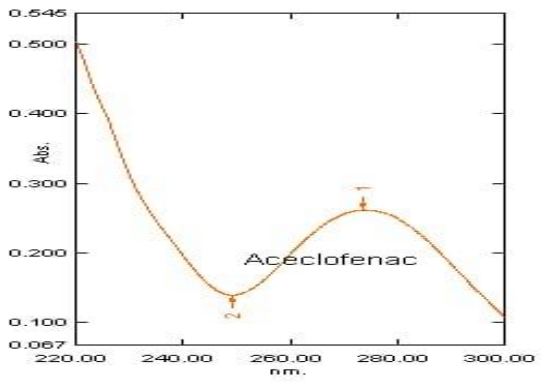

Fig. 1: λmax of Aceclofenac

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 1896-1904 www.ijprajournal.com ISSN: 2456-4494

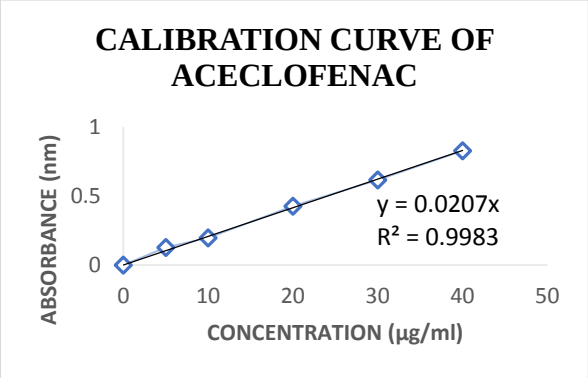

Fig.2: Calibration curve of Aceclofenac

b) Preparation of calibration curve

A standard calibration curve for the drug was obtained by measuring absorbance of the solution (5-40 µg/ml) at 273 nm by plotting the graph of absorbance vs concentration. The calibration plot of Aceclofenac and the obtained coefficient is shown in fig.2.

Table 2: Standard calibration curve of Aceclofenac in pH 6.8 phosphate buffer

S. No.	Concentration(µg/ml)	Absorbance(nm)
1	0	0
2	5	0.128
3	10	0.2336
4	20	0.4251
5	30	0.6166
6	40	0.8259

4.2 COMPATABILITY STUDIES

The FTIR spectra of Aceclofenac and its physical mixture showed no significant interaction between drug and polymers. The FTIR spectra's of Aceclofenac and physical mixture are shown in fig. 3, 4 and 5.

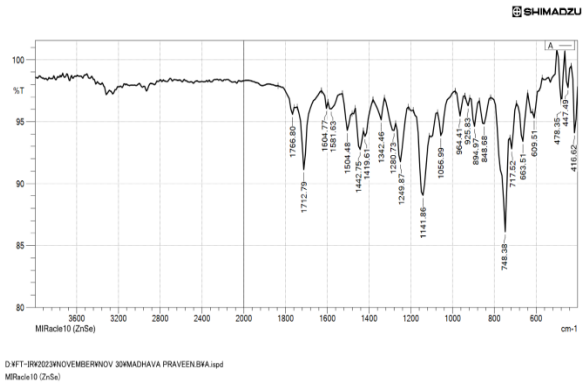

Fig. 3: FTIR spectra of Aceclofenac

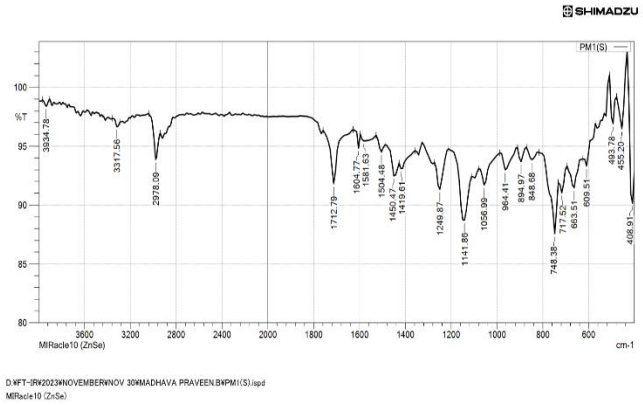

Fig.4: FTIR of SF1

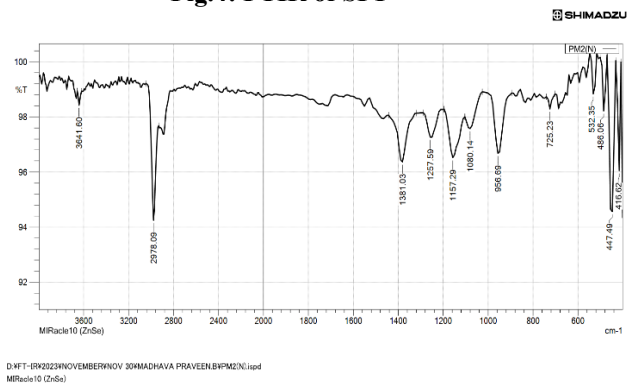

Fig.5: FTIR of NF1

4.3. PREFORMUATION STUDIES

4.3.1. Organoleptic properties:

Organoleptic properties of the drug sample were found to be as given in table below.

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 1896-1904 www.ijprajournal.com ISSN: 2456-4494

Table 3: Organoleptic properties of Aceclofenac.

Parameters	Reported value	Observed value
Colour	White powder	White powder
Crystalline	Crystalline in nature	Crystalline in nature
Taste	Slightly bitter in taste	Slightly bitter in taste
Odour	odourless	odourless

4.3.2. Melting point Determination:
Melting point of Aceclofenac was determined by capillary method. The melting point of Aceclofenac was found to be 148^0, which complied with IP standard, including purity of the drug sample.

.3.3. P^H Determination:
PH was found to be 7.1 ,which complied with IP standard, including purity of the drug sample.

4.3.4. Loss on Drying:
loss on drying of API was found to be 0.03% of its original weight.

4.3.5. Determination of solubility:
Results of solubility of the drug in different solvents are given below in table,

Table 4: Solubility of Aceclofenac in various solvents

Solvents (5 ml)	Solubility of the drug (5 mg)
Distilled water	Insoluble
0.1N HCL	Slightly soluble
6.8 PH Buffer	Poorly soluble
7.4PH Buffer	Slightly soluble
Ethanol	Slightly soluble

4.3.6. Determination of Angle of repose, Bulk density, Tapped density, Carr's index and Hausner's ratio

Table 5: Determination of powder flow property

Batch code	Angle of repose	Bulk Density (gm/ml)	Tapered density (gm/ml)	Carr's Index (%)	Hausner's ratio
SF1	23.96°± 0.21	0.556±0.012	0.564±0.022	6.74±0.24	1.014
SF2	24.97°± 0.26	0.552±0.101	0.592±0.09	7.52±0.19	1.072
SF3	25.21°± 0.14	0.558±0.091	0.608±0.110	5.53±0.26	1.034
NF1	23.81°± 0.26	0.575±0.204	0.608±0.016	7.26±0.25	1.057
NF2	23.86°± 0.18	0.585±0.014	0.614±0.024	7.37±0.26	1.049
NF3	23.89°± 0.16	0.607±0.014	0.615±0.071	5.46±0.29	1.013

*Each value is an average of three determinations
SD – standard deviation.(n=3)

The angle of repose for the formulated granules was carried out and the results were shown in table no.10. It concludes all the formulations blend was found to be in the range 23.86^0 to 25.21^0.

Compressibility index was carried out, and it was found between 5.53% and 7.52% indicating the powder blend has the required flow property for compression.

Hausner's ratio values were found below 1.25, indicating the powder blend has the good flow property.

After the evaluation of granules according to the procedure and table no.6. The tablets were prepared by Direct compression method.

4.4 POST FORMULATION STUDIES

4.4.1. Determination of weight variation, Hardness, Thickness, Friability, % Drug content and surface pH

Table 6: Evaluation of Physical parameters of the formulated tablet

Batch code	Evaluation parameters					
	Weight variation(gm)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	% Drug content	Surface pH
SF1	249.8± 2.16	9.16± 0.08	3.96± 0.08	0.30	98.75± 0.54	6.98
SF2	251.6± 2.38	8.32± 0.81	3.95± 0.09	0.33	98.71± 0.612	6.89
SF3	250.2± 1.39	10.57 ±1.38	3.96± 0.10	0.32	98.72± 0.49	6.94
NF1	249.67 ±1.98	9.78± 1.33	3.97± 0.08	0.32	98.69± 0.51	6.96

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 1896-1904 www.ijprajournal.com ISSN: 2456-4494

NF 2	249.85 ±1.55	9.17± 0.81	3.96± 0.12	0.33	98.54± 0.44	6.92
NF 3	251.45 ±2.03	9.51± 0.86	3.96± 0.09	0.32	98.71± 0.39	6.89

* Each value is an average of three determinations SD - standard deviation(n=3)

The measured hardness of tablets of each batch ranged between 8.32 to 10.57 kg/cm^2, which ensures good handling characteristics of all batches.

The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable.

All the formulated tablets passed weight variation test as the % weight variation was within the pharmacopeial limits of ±7.5% of the weight.

The percentage of drug content for the formulated tablets were found between 98.54% to 98.75% of Aceclofenac, which complies with official specifications.

4.4.2. Determination of swelling index

Table 7: Swelling index of the formulated tablets

Batch code	% Swelling index					
	0.5 hr.	1hr.	2hrs	4hrs	6hrs	8hrs
SF1	33.31	51.29	74.71	88.53	99.28	111.98
SF2	35.71	56.37	77.92	90.18	101.20	120.35
SF3	34.86	56.81	77.98	91.30	101.67	123.89
NF1	32.91	52.14	75.41	89.16	99.82	112.32
NF2	33.12	52.32	76.54	89.81	100.54	121.68
NF3	33.43	52.41	77.67	90.12	101.76	124.01

From the results it was concluded that swelling increases as the time passes because the polymer gradually absorb water due to hydrophilicity of polymer.

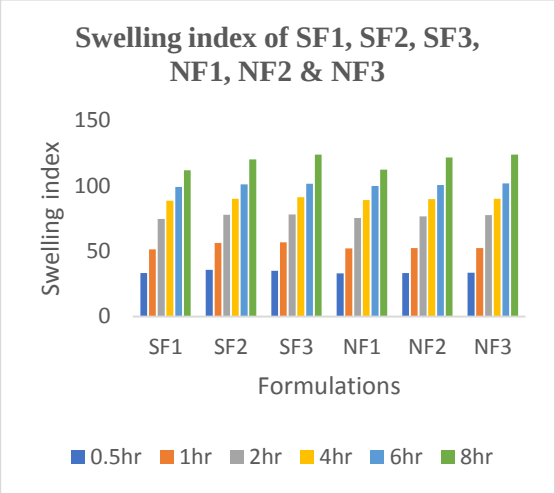

Fig.6: Surface pH of SF1,SF2,SF3,NF1,NF2 & NF3

4.4.3. Determination of Invitro drug dissolution studies

Table 8: Invitro drug dissolution studies of the formulated tablets

Time (Hours)	Cumulative percentage drug release					
	SF1	SF2	SF3	NF1	NF2	NF3
1	6.57	3.56	3.67	12.33	12.49	12.83
2	10.91	7.25	7.43	18.69	18.81	18.83
3	14.49	11.43	11.35	24.76	24.89	26.01
4	20.01	14.37	14.34	30.13	32.45	34.78
5	29.98	17.89	17.78	36.76	38.95	49.34
6	36.81	21.01	19.02	42.56	44.69	45.99
7	41.13	25.24	24.97	48.88	49.97	50.24
8	47.91	29.89	28.63	54.78	56.97	58.29

The batches containing CP and HPMC (SF1-SF3), showed the effective sustain release property but the drug release was ineffective in SF2 and SF3. SF1 satisfied the condition of mucoadhesive strength, sustained and effective release.

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 1896-1904 www.ijprajournal.com ISSN: 2456-4494

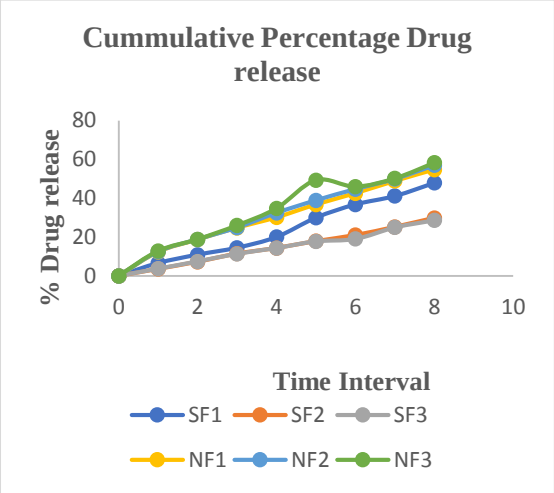

Fig.7: Percentage Drug release of SF1,SF2,SF3,NF1,NF2 & NF3

V. SUMMARY AND CONCLUSION

The development and evaluation of buccal tablets containing Aceclofenac, a nonsteroidal anti-inflammatory drug (NSAID), have been carried out. The buccal route of drug administration offers several advantages, including avoidance of the first-pass metabolism and improved patient compliance. The tablets were formulated to provide sustained release of Aceclofenac, aiming for prolonged therapeutic effects and reduced dosing frequency.

Various excipients were selected to optimize the tablet properties, ensuring good mechanical strength, controlled drug release, and compatibility with buccal administration. The formulation underwent rigorous testing, including in vitro drug release studies and characterization of pharmaceutical parameters.

Results from the studies indicate that the developed buccal tablets of Aceclofenac exhibit promising properties. The drug release profiles demonstrate sustained release characteristics, which could lead to improved patient outcomes and reduced side effects associated with frequent dosing.

Among 3 different batches of synthetic and natural polymers, Natural polymers incremented the drug release rate from the tablet and decremented the dissolution and disintegration time, which reduces the sustained release property of the tablets. Hence synthetic polymers are more suitable for the formulation of mucoadhesive buccal tablets of Aceclofenac.

Among the 3 batches of the formulations with synthetic polymers, SF1 showed sustained and effective drug release, swelling index. Its physicochemical properties also complied with the pharmacopeial standards. Thus, this formulation was considered to be effective to meet all the criteria of mucoadhesive tablet. Moreover, this study also suggested that HPMC can play a significant role to regulate the swelling behaviour, bio adhesion force, and drug release rate of the tablet. Although it has moderately swelling property, it enables steady entry and entrapment of liquid in the polymeric network, which is very significant to achieve sustained release of the drug.

The formulation of an Aceclofenac mucoadhesive tablet can be an effective alternative route to prevent the first-pass effect and to improve the bioavailability of Aceclofenac through the mucosal membrane. It can also enhance patient compliance by fascinating sustained release of the drug.

REFERENCES

[1]. Chien Y, "Novel drug delivery system" 2nd ed. New York: Marcel Dekkar, 2005, 197-198.
[2]. D. Bhowmik, B. Chiranjib, K. Pankaj, R.M. Chandira, Fast dissolving tablet: an overview, J. Chem. Pharm. (2009);1 (1), 163.
[3]. P.C. Reddy, K.S. Chaitanya, Y.M. Rao, A review on bioadhesive buccal drug delivery systems: current status of formulation and evaluation methods, DARU J. Pharm. Sci. (2011);19 (6), 385.
[4]. B. Çelik, Risperidone mucoadhesive buccal tablets: formulation design, optimization and evaluation, Drug Des. Dev. Ther. 11 (2017) 3355–3365.
[5]. B.M. Boddupali, Z.N.K. Mohammed, R.A. Nath, D. Bhanji, Mucoadhesive drug delivery system: an overview, J. Adv. Pharm. Technol. Res. (2010);1(4), 381–387.
[6]. S. Kannan, R. Manivannan, K. Ganesan, P.K. Nishad, N.S. Kumar, Formulation and evaluation of sustained release tablets of aceclofenac using hydrophilic matrix system, Int. J. Pharm. Tech. Res. 2 (3) (2010) 1775–1780.
[7]. Santosh Koirala, Prabin Nepal, Govinda Ghimire, Rojina Basnet, Formulation and evaluation of mucoadhesive buccal tablets of Aceclofenac. Helion 7 . (2021), 2.
[8]. Shivani Kala, Divya Juyal, Preformulation and characterization studies of aceclofenac active ingredient, The Pharma Innovation Journal. (2016); 5(9): 112.
[9]. Himabindu Peddapalli, Vasudha Bakshi, Narender Boggula.,." Formulation, in vitro and ex vivo characterization of mucoadhesive

buccal tablets for antihypertensive drug". Asian Journal of Pharmaceutical and Clinical Research. 2018;11 (8).

[10]. Amrutha JV." Pre and Post Compression Studies of Tablets". Inorganic chemistry: An Indian Journal. 2016 ;11(4).