Journal of Advanced Biomedical and Pharmaceutical Sciences

JABPS

Journal
Of Advanced Biomedical
And Pharmaceutical Sciences

Formulation and evaluation of buccoadhesive films of lidocaine hydrochloride

Gamal M. Mahrous[1], Gamal Shazly[1,2*], Diaa Eldin Zidan[1], Aly A. Abdel Zaher[2], Mona El-Mahdy[3]

[1] Department of Pharmaceutics, College of Pharmacy, King Saud University, PO Box 2457, Riyadh 11451, Saudi Arabia
[2] Department of Industrial Pharmacy, Faculty of Pharmacy, Assiut University 71526, Assiut, Egypt
[3] Department of Pharmaceutics, Faculty of Pharmacy, Assiut University 71526, Assiut, Egypt

Abstract

Buccal delivery is considered the most suitable, easy, and safest route of administration. So it can be used as an alternative route to the peroral route for the systemic administration of drugs. Oral films (OFs) are used as a unique approach, because it dissolves quickly in the mouth and directly reaches to the systemic circulation. The aim of this study is to formulate and evaluate an anesthetic drug lidocaine (LH) and improve its local effect. Oral films were prepared by using chitosan and polyvinylpyrolidone. OFs were assessed for compatibility studies, surface pH, swelling properties, In-Vitro bioadhesion, mechanical properties, disintegration time, dissolution time and in- vitro drug release. It was found that actual LH content in the prepared patch was in the range of 95-105 % of the claimed content. The addition of propylene glycol as a plasticizer gave good mechanical properties in concentration of 40 %. The prepared oral films swelled and reached an Equilibrium state of swelling. The prepared polymeric films showed good adhesion and acceptable pH. It could be concluded that the release of LH is higher from films contain 1 % chitosan. Increasing chitosan concentration to 2 % resulted in decreasing the initial dissolution rate. The combination of chitosan (2 %), PVP (10 %) and PG at 40 % w/w gave a reasonable LH release.

1. Introduction

The drug administration via the oral route is the most preferred route because it is characterized by patient acceptability and compliance, its ease of administration, its non-invasiveness, its adaptability, great stability, dose accuracy and modified drug release profile leading to prolong or delay the drug effect, as well as to enhance drug release [1]. On the other hand, using the solid oral dosage forms in therapy is quiet related to many exciting problems. Difficulty with swallowing, which occurs in geriatric or pediatric patients is one of these problems [2]. Therefore, buccal drug-delivery systems can be used as a substitute to tablets, capsules and syrups for pediatric and geriatric patients who complain of difficulties in swallowing of oral solid dosage forms [3]. These dosage forms are adhesive tablets, gels, patches, Orally Polymeric Fast Disintegrant Film and oral films. An attractive route of administration is the buccal cavity. There are many vascularizations in the oral mucosa, so it offers higher permeability to many drugs [4]. Buccoadhesive drug delivery systems have increased significant attention with regard to systemic delivery of drugs, which undergo extensive hepatic first pass metabolism [5]. Buccal drug delivery has many advantages compared to other routes of drug administration, e.g. rapid onset of action, high patient acceptance and avoidance of the pain associated with injections [3].

Oral films (OFs) are really dissolving films to administer drugs by adsorbing them in the mouth either buccally or sublingually. These films are basically prepared from hydrophilic polymers that dissolve rapidly on the tongue or in the buccal cavity [6]. The injury of the epithelial tissue, local trauma, aphthous stomatitis, and some viruses are the causes of oral ulcer leading to loss of surface tissue and necrosis [7]. Mouth ulcer may be treated symptomatically by smoothing or removing the local cause of trauma. The local anesthetics can be the choice of medications for releasing pain of mouth ulcers.

Due to the fast onset of action and the intermediate duration of efficacy of lidocaine, it is usually used as a local anesthetic in dental surgeries [8]. Lidocaine has been used to treat the mouth ulcers due to its excellent local anesthetic effect that leads to relieve the pain of the mouth ulcer [9]. OFs of Lidocaine are a unique method for the mouth ulcer treatment and may act as a substitute to ointments, mouth washes and gels for pain relief of oral ulcers. These films release lidocaine very rapidly at the site of action. Moreover, these films are very easy to be used and are suitable for geriatric, pediatric, bedridden patients [10].

Lidocaine, lignocaine, is used to anesthetize the tissue in a defined area and so it is called local anesthetics [11]. Usually, lidocaine is used parenterally in the gum and this causes pain to patients [12]. To avoid that lidocaine is better to be used as oral film.

Therefore, the objective of this study was to formulate lidocaine as buccoadhesive films and to evaluate their mechanical, physical and release profile.

2. Materials and methods

---

* Correspondence: Gamal Shazly
Tel.: +00966590447099; Fax: +20 862345631
Email Address: gaahmed@ksu.edu.sa

2.1. Materials

Lidocaine Hydrochloride (LH) was purchased from MEDEX Co., Naseby, Northlands. Chitosan (CH), high viscosity grade, was purchased from BDH Co., Poole, England. Polyvinylpyrolidone K90 (PVP) was obtained from Serva GmbH & Co., Heidelberg, Germany, propylene glycol (PG) was purchased from BDH Co., Poole, England. All other chemicals used in this study were of analytical grade and were used without further purification.

2.2. Methods

2.2.1. Compatibility studies of LH with the used additives

2.2.1.1. Differential scanning calorimetry (DSC)

To investigate any possible interactions between the drug and the utilized buccoadhesive materials, Differential scanning calorimetry (DSC) was achieved on lidocaine HCl, Chitosan, PVP, and physical mixtures of lidocaine (1:1) with these polymers using Perkin Elmer DSC8000. The samples, each weighing between 5 and 7 mg were weighed into aluminum pans and sealed. DSC runs were performed at a heating rate of 5 °C/min over a temperature of 25–400 °C. Peak temperature, glassy transition and heat of fusion were determined in every sample using the software [13].

2.2.1.2. Preparation of polymeric films containing LH, cast from hydroalcoholic solvent

Polymeric films composed of CH (as bioadhesive polymer) and PVP K90 as the film forming polymer in addition to PG as a plasticizer, were prepared. 10 % PVPK90 solution (dissolved in ethanol) was mixed with a mucoadhesive polymeric hydrogel that was prepared by dispersing the polymer in 1% acetic acid using the variable speed mixer, under constant stirring (600 rpm) fitted with four bladed paddles at room temperature. The samples were stored for at least 24 hrs in the dark at 4-8 °C before casting to ensure total hydration of the polymers and to exclude entrapped air. PG was used as plasticizer at concentrations up to 40 % w/w of polymer content, thus protecting the polymeric films from being brittle upon storage. Before pouring on Teflon coated molds (79.7 cm^2, area), the resulted polymeric gels were brought back to room temp (25 °C). The aqueous (hydroalcoholic) polymeric hydrogels were dried at 38±0.5 °C in an oven for 48 h and then stored in a desiccator at room temperature after Warping in sealed plastic sheets.

The same procedure was adopted for the medicated films after dissolving LH and other additives (Saccharin Sodium 0.1 %) in the hydroalcoholic solution of PVP. A list of formulations is presented in **(Table1)** [14].

2.2.1.3. Spectrophotometric Scanning of LH in presence of the used polymers

A specified concentration of LH in phosphate buffer pH 6.8 was scanned spectrophotometrically at 200-400 nm to determine the wavelength of maximum absorption (λmax). UV spectrophotometric Scanning of LH solution in presence of polymer solutions in phosphate buffer pH 6.8 was also investigated at the same wavelength intervals.

2.2.1.4. Construction of LH calibration curve

LH was determined spectrophotometrically at λ 263 nm. Calibration curve was constructed in the range of 50-400 ug/ml by serial dilutions of stock solution of lidocaine hydrochloride (1 mg/ml). Phosphate buffer solution of pH 6.8 was used in preparation of the stock and serial dilutions.

2.2.1.5. Determination of actual LH content in the prepared films

A specified weight of the prepared films was dissolved in 100 ml phosphate buffer (pH 6.8). Then an aliquot was withdrawn and filtered through a Millipore filter (0.45 um). The filtrate was diluted and the concentration of the drug was determined spectrophotometrically at λ 263 nm [14].

2.2.1.6. Determination of the physico-mechanical properties of the prepared films

Dried film sample of (450+50 μm) thickness was cut to uniform size 2.5x6 cm using a sharp razor blade. Two pieces of cardboard (1x2.5 cm) were attached to the upper and lower end of the film using cyanoacrylate resin adhesive. Attachment of the film to the cardboard facilitated clamping of the film jaws of the load deformation machine (INSTRON model no. 5965), thus preventing pressure on the film prior to, and slipping during application. The film on the cardboard (exposed area to stress equals (4.0x2.5 cm) was clamped between the two jaws of the machine. The upper jaw was movable and the lower was fixed. The load automatically applied to the film was gradually increased and the corresponding magnitude of elongation was recorded until the break point of the film reached. Both film breaking load and percentage of elongation was determined. The tensile strength (TS) of the film was calculated from the breaking load and cross sectional area of the film [15].

The percent of elongation was calculated according to the following equation:

$$\% \text{ of elongation (E/B)} = L_s\text{-} L_o/ L_o \times 100 \qquad \text{(Eq. 1)}$$

Where: -

L_o=original film length

L_s=film length after elongation

The modulus of elasticity (EM) of the film was calculated according to Equation:

$$EM= TS/ (L_s/ L_o) \qquad \text{(Eq. 2)}$$

Each experiment was performed in duplicate and the mean value was taken.

2.2.1.7. Swelling behavior of the prepared Lidocaine polymeric films

The study examined the hydration of the different polymeric films used when placed in contact with artificial saliva. Using a pastry cutter, samples (25 mm^2) of each polymeric film were cut and then weighed by one scale before and after wetting with artificial saliva. The polymeric film sample was placed in a Petri dish, artificial saliva (0.1 ml) was added onto the surface of the polymeric film using a micropipette, and then incubated in one dissector at room temperature. The wetted film was removed at each observation point at time intervals of (5, 10, 15, 30 and 60 min), where the surface was gently dried using blotting paper and weighed again. For each observation point, the test was repeated five times. The hydration percentages of the wet polymeric films were calculated according to the following equation.

$$\text{Hydration (\%)} = (W_H - W_D)/W_D \ x100 \qquad (Eq. 3)$$

Where W_H and W_D represent the weight of the hydrated and dried polymeric films respectively.

2.2.1.8. Determination of surface pH of the prepared films

The surface pH of the prepared films was determined after soaking each formula (1 cm^2 of film) in distilled water (1 ml) for 15 minutes. After the time of soaking the pH of the wet surface was measured by placing the electrode in contact with the surface of the film.

2.2.1.9. In-Vitro bioadhesion test of the prepared films

In vitro bioadhesion of the formulations was examined adopting previously published method [15] using a chicken pouch as a model mucosal membrane. The tissue was obtained from chicken after slaughter, removed from its contents and surface fats, and stored frozen in simulated saliva solution (2.38 g $Na_2HPO_4.2H2O$, 0.19 g KH2 PO4 and 8.0 g NaCl /L, pH= 6.75). This membrane was thawed to room temperature before use.

Rectangular piece (Surface area 4.0 cm^2) of the tissue was cut and glued with cyanoacrylate adhesive on the ground surface of the two tissue holders made of Plexiglas. Four cm^2 of the buccal film was placed between the two tissue surfaces put in contact with each other with uniform and constant light pressure between fingers for one minute to facilitate adhesion bonding. The upper tissue holder was allowed to hang on an iron stand with the help of an aluminum wire fastened with a hook provided on the backside of the holder. A pre weighed light weight polyethylene bag was attached the hook on the back side of the lower tissue holder with aluminum wire. After a pre-load time of 1.0-minute water was added to the polyethylene bag through an intravenous infusion set at a rate 2.0 drops per second until the lower tissue detached by the heavy weight of water infused. The water collected in the bag was measured and expressed, as weight (gram force) required for the detachment [16].

$$\text{Detachment force (dyne/cm}^2) = M \times g \ /A \qquad (Eq.4)$$

Where: -

$\qquad M$ = mass of water infused at the detachment
$\qquad g$ = acceleration due to gravity (981cm/sec^2)
$\qquad A$ = the area of the exposed tissue in cm^2

2.2.1.10. In – vitro release studies of the prepared LH buccal films

The in-vitro release of LH from the prepared films was investigated using the USP Apparatus 2. The previously prepared film was removed from the plate, weighed on an analytical balance, and the thickness was measured at both the four corners and the center with a micrometer. The film was carefully pressed on and adhered to a Plexiglas disk. The temperature of the dissolution medium (300 ml of phosphate buffer pH 6.8) was adjusted to 37+0.5 °C. The Plexiglas support containing the film was placed in the bottom of the vessel, and then the paddles of the dissolution tester were allowed to rotate at 50 rpm which was the optimum speed to prevent film rupture. It was taken into consideration that the used buffer volume affords sink conditions. Samples (5 ml each) were obtained at time intervals while the film completely immersed throughout the release study. The removed sample (5 ml) from the release medium was replaced by an equal volume of buffer. The run was continued for 3 hours. All samples were analyzed spectrophotometrically at 263 nm. Blank samples were obtained from the release experiments of patches containing the same components except the drug [14].

Analysis of the release data

The release data were kinetically analyzed using different Kinetic models (Zero order, first order and Higuchi diffusion model) to determine the mechanism of HZ release from the different Buccal film formulations [17].

3. Results and Discussion

3.1. Compatibility studies

Differential scanning calorimetry (DSC) studies were achieved to examine the physical interactions between lidocaine and the components used in the film. The DSC thermogram of pure lidocaine (**Figure 1**) exhibited a melting endotherm at 80.22 °C with a heat of fusion of 110.80 J/g. In the thermogram of pure chitosan (**Figure 1**), there is a broad endotherm ranging from about 90 to 110 °C [17]. The thermogram of pure PVP (**Figure 1**) showed a broad endotherm ranging from about 85 to 130 °C due to the presence of water [18]. The physical mixture of lidocaine–chitosan (1:1) (**Figure 1**) displayed the same melting peak of lidocaine with the loss of its sharp peak due to decrease the amount of lidocaine and replacing it with chitosan carrier. The same results were obtained with lidocaine–PVP physical mixture (1:1). From these results we can exclude the possibility of interaction.

3.2. Spectrophotometric Scanning of Lidocaine in presence of solutions of the polymers used to prepare films

Results of Spectrophotometric Scanning of LH in phosphate buffer pH 6.8 showed that there is a maximum absorption wavelength at 263 nm. In the presence of solutions of the polymers used to prepare films, no interference has been detected by the spectrophotometric analysis of the drug at 263 nm.

3.3. Calibration curve of LH in phosphate buffer pH 6.8 at 263 nm

A linear relationship between the absorbance and the concentration of LH in phosphate buffer pH 6.8 at 263 nm was obtained in a concentration range of 50-400 ug / ml. The regression equation is y = 0.0016x and r value is 0. 9999.

3.4. Determination of actual LH content in the prepared films

Actual LH content in the prepared films was in the range of 95-105 % of the claimed content. This indicates the stability of LH in the used procedure for preparation as well as the even distribution of the drug in the prepared films.

3.5. Physico-mechanical properties of the prepared films

An ideal buccal film should be flexible, elastic, soft, adequately strong to withstand breakage due to stress from mouth activities. Moreover, it must also possess good bioadhesive strength so that it can be retained in the mouth for a desired duration. Swelling of film should not be too extensive to prevent discomfort. As such, the mechanical, bioadhesive, and swelling properties of buccal film are critical and essential to be evaluated.

Mechanism of film formation

For the preparation of polymeric films containing drugs, drugs were dissolved in the polymer solution prior to casting. The concentration of solute is very important in preparation of the polymer matrix. The solution was kept at room temperature for 24 hrs. In order to enhance interpenetration of polymer particles. Upon drying, polymer solutions were converted into drug polymer films. Various research groups have studied the mechanism of film formation from polymer dispersions [11]. The film formation occurs in three stages:

(i) Evaporation of casting solvent and subsequent concentration of polymer particles.

(ii) Deformation and coalescence of polymer particles.

(iii) Further fusion by interdiffusion of polymeric molecules of adjacent polymer particles. The physical state of the drug in the dried film is dependent on the solubility of the drug in the polymer. A prerequisite for the successful preparation of the films was the compatibility of the dissolved drug and the used polymers. All polymers used were found to be compatible with the drug.

3.5.1. Mechanical properties

The tensile testing gives an indication of the strength and elasticity of the film, reflected by the parameters tensile strength (TS), elastic modular (EM) and elongation at break (E/B). A soft and weak film is characterized by a low TS, EM and E/B, a hard and brittle film is defined by a moderate TS, high EM and low E/B, a Soft and tough film is characterized by moderate TS, low EM and high EIB, whereas a hard and tough film is characterized by a high TS, EM and E/B [13]. Hence it is suggested that a suitable buccoadhesive film should have a relatively moderate TS, E/B and strain but a low EM.

A) Non-medicated films (NM)

Several trails were made to reach the required mechanical properties for buccal films (soft and tough), using PVP as a film forming polymer which is widely accepted in preparation of buccal films. Mucoadhesive polymer used was chitosan. Non plasticized formulae were all hard and brittle. Addition of PG as plasticizer gave good mechanical properties in concentration of 40 % in all trials **(Table 1)**. It is clear from **(Table 1)** that the film formula (NM4) is soft and tough.

B) Medicated films

(Table 1) shows the composition and the mechanical properties of the prepared LH films. The inclusion of LH in the prepared films reduced the EM and TS which could be attributed to the weakening of the polymer intermolecular binding by the presence of the drug allowing the polymer to move more freely resulting in an increase in the flexibility of the medicated films. Addition of PG as plasticizer gave good mechanical properties in concentration of 40 %.

3.5.2. Swelling Studies of the prepared LH films

The swelling behavior of the polymer was reported to be crucial to its bioadhesive character. The adhesion occurs shortly after the beginning of swelling, but the bond formed is not very strong. The adhesion will increase with the degree of hydration until a point where over hydration leads to an abrupt drop in adhesive strength due to disentanglement at the polymer tissue interface. The rate and extent of film hydration and swelling will also affect the drug release from the film. Some degrees of hydration appear to be beneficial to bioadhesion [19]. An examination of the hydration rates of polymeric films with different bioadhesive characteristics might be helpful to explore the mechanism underlying bioadhesion. Accordingly, after beginning the swelling test (5 min), the prepared polymeric films swelled and reached an equilibrium state of swelling **(Table 2)**. Incorporation of LH decreased water uptake behavior of the prepared films but not in a significant way that affect the adhesion properties.

3.5.3. In vitro Bioadhesion studies of the prepared LH films

There are several advantages in having bio/mucoadhesive drug delivery systems. As a result of such adhesion, the formulation stays longer time at the delivery site and this increase the duration of the effect. Also the increased residence time will enhance and prolong the local effect of the drug whenever it is desired. So, the bioadhesive force is an important physicochemical parameter for buccoadhesive dosage forms. **(Table 3)** shows the results of bioadhesion tests for different polymeric films and showed good adhesion and acceptable pH. Incorporation of LH in the films causes a slight decrease in mucoadhesive properties of the investigated film formulations.

3.6. In-vitro release studies of the prepared LH films

The in-vitro release of the drug from buccal films contains LH (formulae F1- F4) was studied at 37 °C using phosphate buffer (pH 6.8) as the release medium. The percent of the drug released as a function of time is presented in **(Figure 2)**.
It could be seen from the results that the release of LH is higher from films contain 1 % chitosan. This could be explained on the basis of rapid and high swelling rate of films. Increasing chitosan concentration to 2 % resulted in decreasing the initial dissolution rate.
The combination of chitosan (2 %), PVP (10 %) and PG at 40 % w/w (F4) gave a reasonable LH release (about 77 % at 1 hour). As concluded before, this formula showed also good adhesion and acceptable pH. These results are in accordance with previous reports used other bioadhesive polymers [20, 21].

3.7. Kinetic Assessment of the in-vitro release data of HZ

In order to determine the release model which best describes the pattern of drug release, the in-vitro release data were fitted to zero order, first order and diffusion controlled release

mechanisms according to the simplified Higuchi model [22]
a) Zero-order Kinetic model: $C = C_o - K_o t$.
b) First Order Kinetic model: $\log C = \log C_o - Kt/2.303$
c) Higuchi diffusion model: $Q = 2 C_o (Dt/\pi)^{1/2}$

Where: -

C_o = initial drug concentration
C = drug concentration (released) at time t.
T = time of release
Q = amount of drug released/unit area
K_o = zero order rate constant, K = first order rate constant and D = diffusion Coefficient and it was calculated according to the following equation.
$D = (\text{Slope}/2C_o)^2 \pi$

The preference of a certain mechanism was based on the correlation coefficient (r) for the parameters studied, where the highest correlation coefficient is preferred for the selection of mechanism of release.
Successive evidence of the relative validity of diffusion and first order models obtained by analyzing the data using the following equation [22]

$Mt/M_{oo} = K. t^n$

Where Mt/M_{oo} is the fraction released by the drug at time t, K is a constant incorporating structural and geometric characteristic and n is the release exponent characteristic for the drug transport mechanism. When n=0.5 fickian diffusion is observed and the release rate in dependent on t, while 0.5<n<1.0 indicate anamalous (non fickian) transport and when n=1, the release is zero order.
The mathematical treatment of the vitro release data of LH from the prepared buccal films are presented in **(Table 4)**. r & n values of these formulation support an anomalous non-fickian release that support a combination of diffusion of the drug and erosion of the film control the release.

Table 1: The Physico-Mechanical Properties of Non Medicated and LH Medicated Polymeric films

	Polymer type and concentration		PG % Polymer	LH mg/cm^2	TS Nmm^{-2}	EM N mm^{-2}	E/B% mm^{-2}	Mechanical observations
	Film forming Polymer	Bioadhesive Polymer						
NM$_1$	PVP 7.5%	CHL 1%	30	-	-	-	-	hard & tough
NM$_2$	PVP 7.5%	CHL2%	30	-	-	-	-	hard & tough
NM$_3$	PVP 10%	CHL 1%	40	-	-	-	-	soft& tough
NM$_4$	PVP 10%	CHH 2%	40	10	1.48	.74	200	soft & tough
F1	PVP 7.5%	CHl1%	30	10	-	-	-	hard& tough
F2	PVP 10%	CHL2%	30	10	-	-	-	hard & tough
F3	PVP 10%	CHH 1%	40	10	-	-	-	soft & tough
F4	**PVP 10%**	**CHH 2%**	**40**	**10**	**0.911**	**0.535**	**170**	**soft & tough**

*CHL: Chitosan Low Molecular Weight; CHH: Chitosan High Molecular Weight; NM: None Medicated films; LH: lidocaine HCl; TS: Tensile Strength; EM: modulus of elasticity; E/B%: The percent of elongation; PG: Propylene Glycol

Mahrous *et al.*

Table 2: Percent Swelling of the Non Medicated and LH medicated polymeric films

Formula no.	% Swelling at times (min):				
	5	10	15	30	60
NM1	12.2±2	20±3	35.2±4.5	48±7.0	66±6
NM2	16.2±2	26±3	40.2±4.5	60±7.0	74±6
NM3	17.2±3.2	28±3.4	40.2±0.2	56.2±5	81.24±5
NM4	13.5±3.5	20.1±3.5	35.1±3.4	70±6.1	90.1±6
F1	12.1±3.6	21±4.0	36±3.6	53±6.2	71±7.2
F2	15.1±3.6	21±4.0	38±3.6	55±6.2	77±7.2
F3	11.2±1.2	17.2±1.5	27.4±3.1	49.2±4.5	86.1±6
F4	**11.5±1.5**	**16.3±1.7**	**28±3.1**	**51.2±4.5**	**84.1±6**

Table 3: Detachment force and surface pH of the prepared films

Formula No.	Detachment force dync/cm^2 x10^{-3}	Surface pH
NM1	26.8 ± 2.8	5.0
NM2	24.2 ± 3.5	5.3
NM3	23.86 ± 4.2	5.8
NM4	21.10 ± 2.8	5.8
F1	23.25 ± 2.2	5.1
F2	21.1 ± 4.3	5.4
F3	22.65 ± 3.8	5.6
F4	**20.66 ± 2.9**	**5.2**

Table 4: Kinetic modeling of drug release form films containing LH (100 mg)

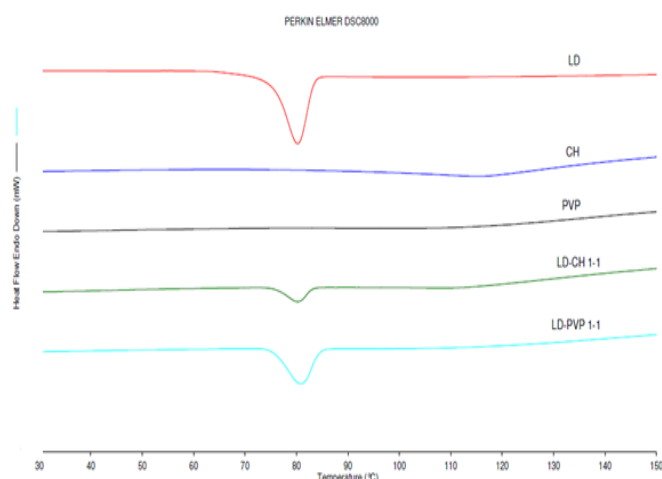| Release Model		Formula No.			
		F1	F2	F3	F4
Zero order	r	0.74678	0.7623	0.7062	0.8022
	Ko (mg/min)	0.4409	0.457	0.4148	0.4335
First order	r	0.9474	0.9424	0.9669	0.9841
	K1 (min-1) x103	5.01	5.12	5.0	3.26
Higuchi diffusion	r	0.9219	0.9267	0.9004	0.9445
	Kh(mg/cm2)/min1/2	7.6476	7.81	7.43	7.247
Log Q Vs log t	r	0.9636	0.959	0.9736	0.9969
	n	0.243	0.297	0.1759	0.2713
Selected models		Non-Fickian diffusion			

Figure 1: DSC thermograms of lidocaine (LD) and its mixtures with the used polymers, Chitosan (CH), Polyvinylpyrolidone (PVP).
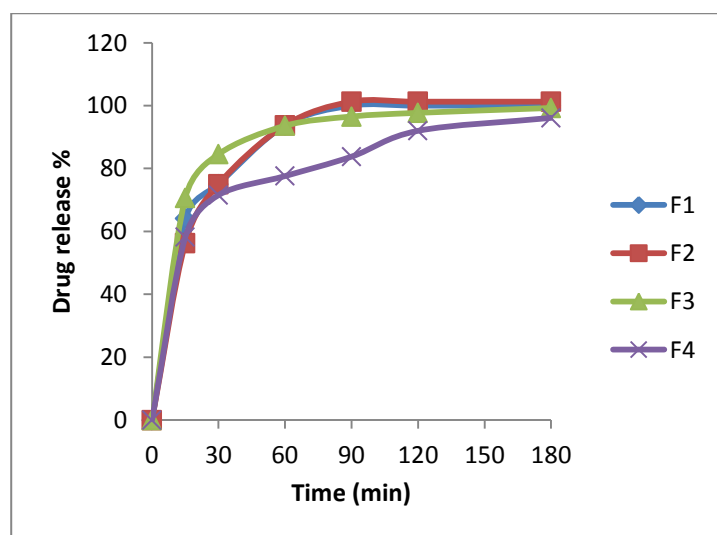

Figure 2: % In vitro release profiles of lidocaine from different formulations in Phosphate buffer pH 6.8.

Conclusion

The prepared polymeric films showed good adhesion and acceptable pH. The addition of propylene glycol as a plasticizer gave good mechanical properties in concentration of 40%. The prepared oral films swelled and reached an Equilibrium state of swelling. It could be concluded that the release of LH is higher from films contain 1 % chitosan. Increasing chitosan concentration to 2 % resulted in decreasing the initial dissolution rate. The combination of chitosan (2 %), PVP (10 %) and PG at 40 % w/w gave a reasonable LH release over three hours expecting an anesthetic effect for a reasonable time.

Acknowledgement

References

[1] Valleri M, Mura P, Maestrelli F, Cirri M, Baller ini R. Development and evaluation of glyburide fast dissolving tablets using solid dispersion technique. *Drug Dev Ind Pharm,* 2004.**30**(5): 525-34.

[2] Nissen LM, Haywood A, Steadman KJ. Solid medication dosage form modification at the bedside and in the pharmacy of Queensland Hospitals. *J Pharm Prac Res,*2009. **39**:129–134

[3] Nagendrakumar D, Keshavshetti GG, Mogale P, Swami S, Swami H, Formulation and evaluation of fast dissolving oral films of metoprolol succinate. *Int J Eng App Sci,*2015. **6**:28–38

[4] Smart JD. Buccal drug delivery.*Expert Opin. Drug Deliv*, 2005.**2**:507–517

[5] Rathbone MJ, Drummond BK, Tucker IG. The oral site as a site for systemic drug delivery. *Adv Drug Deliev Rev,* 1994.**13**:1–22.

[6] Godbole A, Josh R, and Sontakke M. Oral Thin Film Technology-Current Challenges and Future Scope. *IJAAS,*2018.**7**(2):1-14.

[7] Sandy H, Michelle M, Chasari T, Katherine L, Andrew D, Franz B. Topical lidocaine to improve oral intake in children with painful infectious mouth ulcers-blinded, randomized, placebo-controlled trial. *Annals Emerg Med*, 2014.**63**: 292-299.

[8] Ahmad J, Andrabi SIH, Rathore MA. Comparison of topical glyceryl trinitrate with lignocaine ointment for treatment of anal fissure: A randomised controlled trial. *Int J Surg,* 2007.**5**: 429-432.

[9] Rana A, Shereen A, Mutaz S &Alsayed S. Mucoadhesive Dosage form of Lidocaine Hydrochloride: I. Mucoadhesive and Physicochemical Characterization. *Drug Dev Ind Pharm*. 2007. **33**(8):855-64.

[10] Chaudhary H, Gauri S, Rathee P, Kumar V. Development and optimization of fast dissolving oro-dispersible films of granisetronHCl using Box-Behnken statistical design. *Bull Facul Pharm Cairo Uni,* 2013.**51**: 193-201.

[11] Quinn RH, Wedmore I, Johnson E, Islas A, Anglim A, Zafren K, et al. Wilderness medical society practice guidelines for basic wound management in the austere environment. *Wild Environ Med,* 2014.**25**:295 –310.

[12] Kim NW, Lee MS, Kim KR, Lee JE, Park JS, Matsumoto Y, et al. Polyplex-releasing microneedles for enhanced cutaneous delivery of DNA vaccine. *J Control Release*, 2014.**179**:11–7.

[13] Marina K, Narayana R, K Vijayanarayana & Prabhakara P. In vitro and in vivo. evaluation of chitosan buccal films of ondansetron hydrochloride. *Int J Pharm Investig.* 2011. **1**(3): 164–171.

[14] Gamal M. Formulation and evaluation of buccoadhesive films of hydralazine hydrochloride. *World J Pharm Res*. 2016. 5(6), 14-30.

[15] Agarwal V., Mishra B. Design, development and biopharmaceutical properties of bucco-adhesive compacts of pentazocine. *Drug Devel. Ind. Pharm,* 1999.**25**:701-709. [16] Korsmeyer, RW, Peppas, NA. Macromolecular and modeling aspects of swelling-controlled systems, in: "Controlled Release Delivery Systems", T. J. Roseman and S. Z. Mansdorf, (Ed.s), Dekker, New York, N. Y., p.77 (1983).

[17] Luciana S, Guinesi É, Tadeu G. The use of DSC curves to determine the acetylation degree of chitin/chitosan samples Author links open overlay panel. *Thermochimica Acta*, 2006. **444**(2):128-133.

[18] Biswal S, Sahoo,J and Murthy P.N. Physicochemical Properties of Solid Dispersions of Gliclazidein Polyvinylpyrrolidone K90. *AAPS Pharm SciTech*, 2009. **10**(2):329-34.

[19] Needleman IG., Martin GP., Smales FC. Characterization of bioadhesives for periodontal and oral mucosal drug delivery.*J Clin. Periodontal*, 1998. *25*:74-82.

[20] M. Ishida, N. Nambu, T. Nagai, Mucosal dosage form of lidocaine for toothache using hydroxypropyl cellulose and carbopol.*Chem. Pharm. Bull(Tokyo),*1982. **30**: 80–984.

[21] Deshpande AA., Shah NH., Rhodes CT., Malick W. Evaluation of film used in development of a novel controlled-release system for gastric retention. *Int. J. Pharm*,1997.**159**: 255-258.

[22] Dorota, W, Pastuszka,1 Justyna K, Bartosz M, Ryszard B, Bogdan O & Witold M. Evaluation of the Release Kinetics of a Pharmacologically Active Substance from Model Intra-Articular Implants Replacing the Cruciate Ligaments of the Knee. Materials, 2019. **12**(8): 1202.