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DEVELOPMENT AND IN-VITRO EVALUATION OF MUCOADHESIVE BUCCAL PATCHES OF DIMENHYDRINATE

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Abstract:
Dimenhydrinate is a H_1 Antagonist; it is used in the treatment of vomiting caused by motion sickness. These controlled release Muccoadhesive buccal patches mainly prepared for release of the drug for longer period of time i.e., 10 hours and utilizing the drug to full extent avoiding unnecessary frequency of dosing. For the formulation of Muccoadhesive buccal patches HPMC E15, HEC, PVAand PVP were used as matrix forming agents. Other excipients used are Propylene glycol as a plasticizer. Fourier transform Infrared spectroscopy confirmed the absenceof any drug/polymers/excipients interactions. The Muccoadhesive buccal patches were prepared by solvent casting method using magnetic stirrer. The prepared controlled release Muccoadhesive buccal patcheswere evaluated for thickness, folding endurance, weight variation, water uptake, bioadhesive strength, drug content uniformity, surface p^H, Mechanical strength, Scanning electron microscopy (SEM), In-vitro release study, Invitro residence time, Ex-vivo drug release study, Stability study and Kinetic study. Formulation F3 showed good Bioadhesive strength and a controlled drug release and also shown good result for all other parameters when compared with all other formulations. Hence formulation F3 is considered to be the optimized formulation. Stability studies were carried out for F3 formulation they had showed good stability when stored at accelerated stability state as per the ICH guideline and the values were with in a permissible limits. It was observed that Formulations F3 retained the drug release up to 24 hrs. All formulations were subjected for four different models viz. Zero order, First order,Higuchi matrix and Peppas model equations and all the formulations best fit in to thePeppas model by giving the values of diffusional exponent (n) in the range of 0.6-0.9that indicate the formulation had release the drug by diffusion followed by erosion mechanism. It was revealed that polymer ratios had significant influence on drug release. Thus conclusion can be made that stable dosage form can be developed for Dimenhydrinate for controlled release by buccal patches.

Key words: Formulation, Evaluation, Mucoadhesive Buccal Patches, Dimenhydrinate

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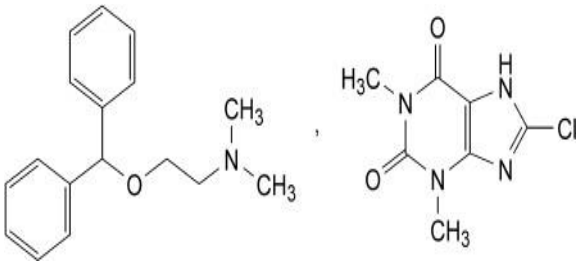
INTRODUCTION:

Amongst the various routes of drug delivery, oral route is perhaps the most preferred to the patient and the clinician alike. However, per oral administration of drugs has disadvantages such as hepatic first pass metabolism and enzymatic degradation within the GI tract, that prohibit oral administration of certain classes of drugs especially peptides and proteins. Consequently, other absorptive mucous membrane are considered as potential sites for drug administration. Transmucosal routes of drug delivery (i.e., the mucosal linings of the nasal, rectal, vaginal, ocularand oral cavity) offer distinct advantages over oral administration for systemic drug delivery. These advantages include possible bypass of first pass effect, avoidance of presystemic elimination within the GI tract, and depending on the particular drug, a better enzymatic flora for the drug absorption1. Amongst the various routes of administration tried so far in the novel drug delivery systems, localized drug delivery to tissues of the oral cavity has been investigated for the treatment of periodontal disease(gum infection), bacterial and fungal infection. Over the decades mucoadhesion has become popular for its potential to optimize localized drug deliveryby retaining a dosage form at the site of action (e.g. within the gastrointestinal tract) or systemic delivery by retaining the formulation in intimate contact with the absorption site (e.g. buccal cavity). Well defined bioadhesion is the ability of a material (synthetic or biological) to adhere to a biological tissue for an extended period of time 2, 3, 4. The biological surface can be epithelial tissue or it can be the mucous membrane adhere on the surface of a tissue. If adhesion is to a mucous coat, the phenomenon is referred to as mucoadhesion. The use of mucoadhesive polymers in buccal drug delivery has a greater application3.Various mucoadhesive devices, including tablets, films, patches, disks, strips, ointments and gels have recently been developed. However, buccal patch offer greater flexibility and comfort than the other devices. In addition, a patch can circumvent the problem of the relatively short residence time of oral gels on mucosa, since the gels are easily washed away by saliva. Buccal route drug delivery provides the direct entry to the systemic circulation through the jugular vein bypassing the first pass hepatic metabolism leading to high bioavailability 5, 6, 7. Other advantages such as excellent accessibility, low enzymatic activity, suitability for drugs or excipients that mildly and reversibly damage or irritate the mucosa, painless administration, easy withdrawal, facility to include permeation enhancer/ enzyme inhibitor or pH modifier in the formulation, versatility in designing as multidirectional or unidirectional release system for local or systemic action8,9,10.

Dimenhydrinate is an over-the-counter drug used to prevent motion sickness. It is closely related to diphenhydramine HCl, or Benadryl. It is primarily a H1- antagonist, but also possesses an antimuscarinic effect.

Structure:



Dimenhydrinate is a member of drug belonging to the class of H_1 anti histamine used in treatment of post operative vomiting. Dimenhydrinate undergoes first pass metabolism in the liver and as a consequence the availability of Dimenhydrinate in general circulation is low and variable.

Physicochemical properties of Dimenhydrinate like small dose lipophilicity, stability at buccal P^H, tasteless odorless and more absorption through buccal mucosa makes it an ideal candidate for administration by buccal route. Hence in the present work an attempt is being made to formulate a buccal mucoadhesive dosage form for Dimenhydrinate in the form of buccal patches by using four different polymers Hydroxy Propyl Methyl Cellulose (HPMC), Hydroxy Ethyl Cellulose (HEC), Poly Vinyl Alcohol (PVA), Poly Vinyl Pyrolidine (PVP) to overcome the Hepatic metabolism and low bioavailability.

METHODOLOGY:

The following materials & instruments were used for the preparation of Dimenhydrinate buccal patches.

Table No. 1: LIST OF CHEMICALS USED

S.no	Name	Grade	supplier
1	Dimenhydrinate	Pharma	Aurabindo pharmaceuticals.
2	HPMC E15	USP/EP	Alkem laboratories
3	Hydroxy ethylcellulose	Laboratory	SD Fine Chemicals Ltd. Mumbai.
4	Poly vinyl alcohol	Laboratory	SD Fine Chemicals Ltd. Mumbai.
5	Poly vinylpyrolidine	Laboratory	SD Fine Chemicals Ltd. Mumbai.
6	Propylene glycol	Laboratory	SD Fine Chemicals Ltd. Mumbai.
7	Potassiumdihydrogen phosphate	Laboratory	SD Fine Chemicals Ltd. Mumbai.
8	Disodium hydrogen phosphate	Laboratory	SD Fine Chemicals Ltd. Mumbai.
9	Distilled water	Laboratory	-----

PREPARATION OF BUCCAL PATCHES:

Patches containing Dimenhydrinate and HPMC E15, HEC, PVP, PVA different proportions was prepared by the solvent casting method. The drug was dissolved in 5ml of methanol and the polymers were dissolved in separate container with 20ml of distilled water under continuous stirring for 4 hours. After stirring, mix the drug and polymer solution. Propylene glycol was added into the solution as a plasticizer under constant stirring. The viscous solution was left over night to ensure a clear, bubble free solution. The solution was poured into a glass petridish and allowed to dry at 40^0c temperature till a flexible patch was formed. Dried patch was removed carefully, checked any imperfections or air bubbles and cut into pieces of $1mm^2$ area. The patches were packed in aluminum foil and stored in desiccators to maintain the integrity and elasticity of the patches. Table no.3 shows the composition of differentbuccal patches.

Table no. 2: composition of buccal patches of Dimenhydrinate.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Dimenhydrinate	250 mg	250 mg	250 mg	250 mg	250 mg	250 mg	250 mg	250 mg	250 mg	250 mg
HPMC E15	750 mg	----	250 mg	375 mg	500 mg	750 mg	----	250 mg	375 mg	500 mg
HEC	----	750 mg	500 mg	375 mg	250 mg	----	750 mg	500 mg	375 mg	250 mg
PVP	125 mg	125 mg	125 mg	125 mg	125 mg	----	----	----	----	----
PVA	----	----	----	----	----	125 mg	125 mg	125 mg	125 mg	125 mg
ETHANOL	5ml	5ml	5ml	5ml	5ml	5ml	5ml	5ml	5ml	5ml
Propylene glycol	0.7 ml	0.7 ml	0.7 ml	0.7 ml	0.7 ml	0.7 ml	0.7 ml	0.7 ml	0.7 ml	0.7 ml
Distilled water	25ml	25ml	25ml	25ml	25ml	25ml	25ml	25ml	25ml	25ml

RESULTS:

Preformulation studies:

Identification of pure drug:

IR Spectroscopy:

The IR spectrum of pure drug of Dimenhydrinate shows the following functional groups at their frequencies. Table No. 3: Interpretation of IR spectra

S.no	Functional group	IR range	Assessment ofpeak(cm^{-1})
1	C-H Stretching in CH_3 group	1020-1220	1041.60
2	C-H Stretching in aromatic ring	3100-3000	3030.27
3	N-H Stretching in Hetero aromaticring	3500-3220	3329.25
4	C-Cl Stretching of mono chlorinated aromatic compound	750-700	702.11
5	C-H Stretching in Methoxy group	2815-2850	2818.09
6	C-H Bending vibration in CH_2 group of R-CH2-N=	1475-1445	1462.09

Calibration curve of Dimenhydrinate in distilled water:

The absorbance of Dimenhydrinate standard solution containing 1-10mcg/ml of drug in distilled water. Graph no shows a representative calibration curve with slope and regression coefficient, 0.018 and 0.999 respectively. The curve was found to be linear in the range of 1-10mcg/ml at absorbance maxima 276nm.

Figure 1: Absorption maxima scanning of Dimenhydrinate.

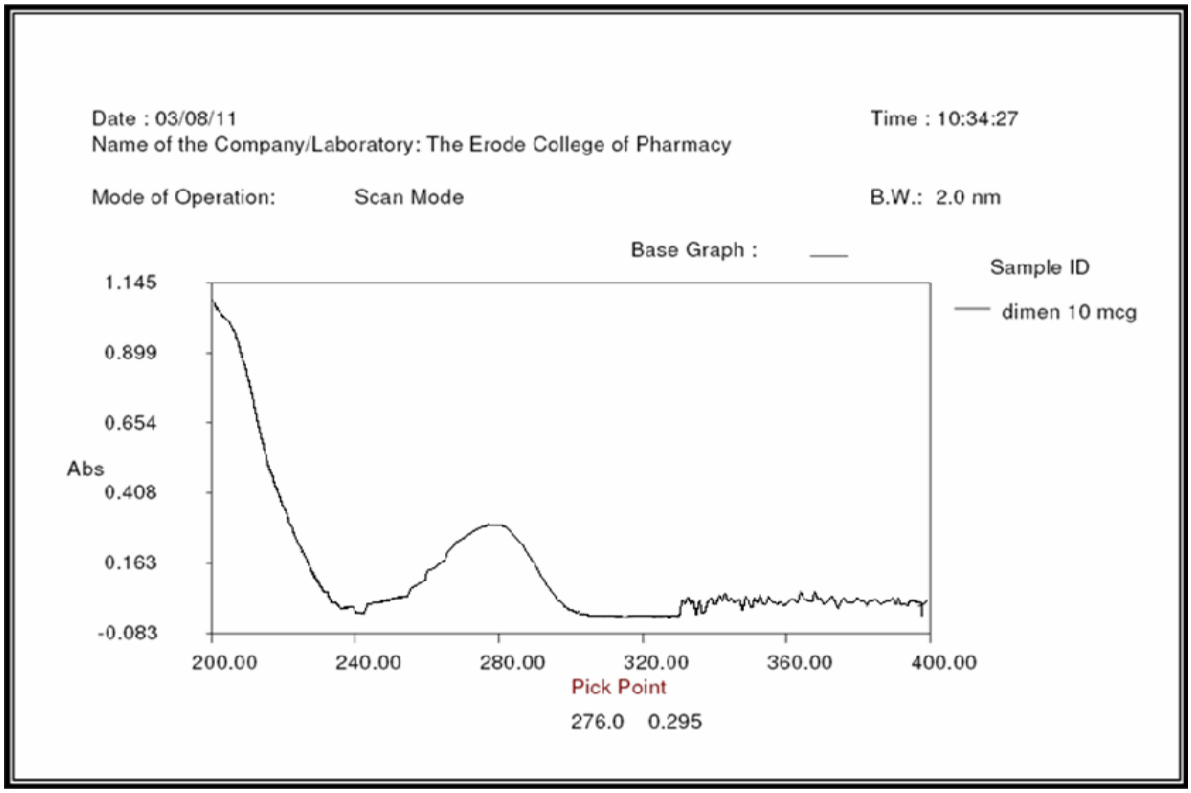
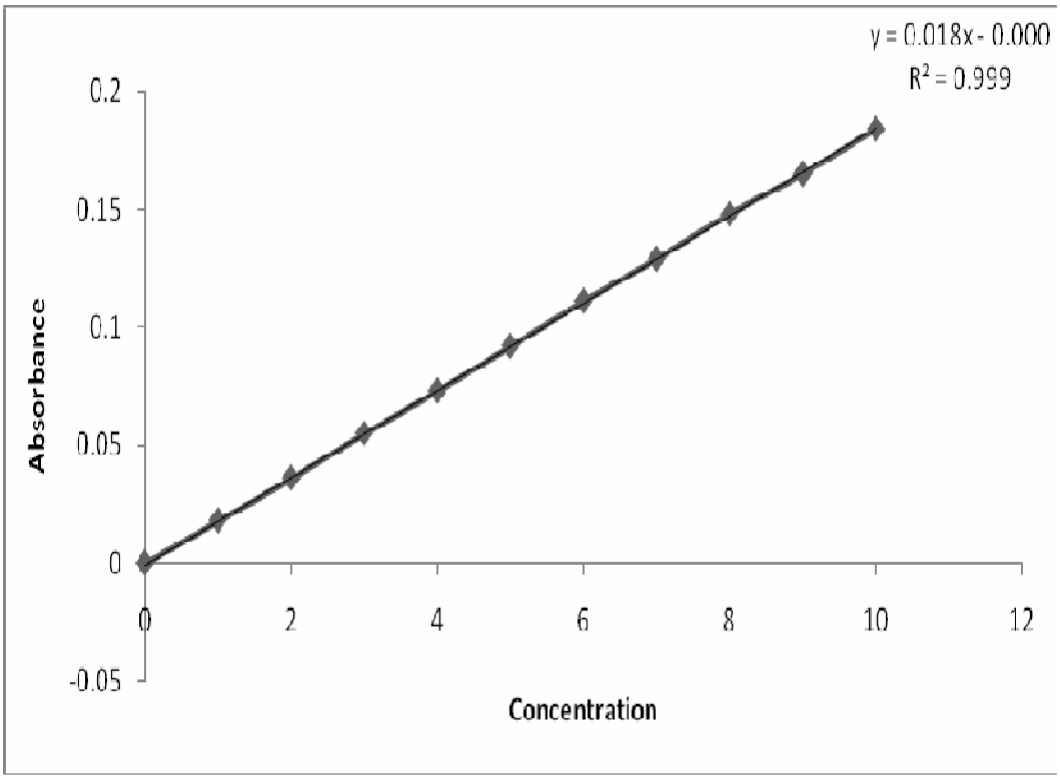


TABLE NO.4: STANDARD CURVE OF DIMENHYRINATE USING DISTILLED WATER.

S.NO	Concentration(mcg/ml)	Absorbance
1	0	0
2	1	0.018
3	2	0.036
4	3	0.055
5	4	0.073
6	5	0.092
7	6	0.111
8	7	0.129
9	8	0.148
10	9	0.165
11	10	0.184

Figure 2: STANDARD CALIBRATION CURVE FOR DIMENHYRINATE IN DISTILLED WATER.



EVALUATION PARAMETERS:

Table.no.5: Evaluation of Physical parameters of different mucoadhesive buccalpatches of Dimenhydrinate.

Formulation code	Physical parameters			
	Thickness (mm) ±S.D (n=3)	Folding endurance ±S.D (n=3)	Mechanical strength ±S.D (n=3) (kg/mm^2)	Wateruptake ±S.D (n=3)
F1	0.23± 0.005	305± 4.04	5.28± 0.076	2.15± 0.64
F2	0.22± 0.014	305± 4.72	6.04± 0.056	2.02± 0.52
F3	0.24± 0.002	313± 2.51	12.94± 0.098	2.93± 0.102
F4	0.26± 0.0023	318± 2.51	12.64± 0.124	2.53± 0.23
F5	0.25± 0.001	302± 1.00	10.86± 0.132	1.95± 0.051
F6	0.23± 0.003	312± 2.51	6.84± 0.079	1.93± 0.153
F7	0.24± 0.023	318± 2.52	7.23± 0.32	2.07± 0.354
F8	0.26± 0.01	310± 5.50	9.45± 0.054	2.18± 0.243
F9	0.26± 0.034	309± 5.51	12.14± 0.045	2.46± 0.109
F10	0.25± 0.023	304± 4.50	11.96± 0.091	2.00± 0.63

Performance parameters:
Content uniformity of active ingredient:

Table shows the result of drug content uniformity in each formulation.Three replicates of each test were carried out. The mean drug content was found to bein the range of 3.68 to 3.8 for (each patch size 10mm diameter) the prepared buccal patch formulations.
Measurement of bioadhesive strength:

An effective buccal mucosal device must maintain an intimate contact with mucus layer overlying the epithelial tissue. This parameter very important to successful utilization of these dosage forms. Hence in-vitro evaluation of buccal patches was carried out using porcine gastric mucosa. This gives the indirect measurement of bioadhesive strength in grams.
Table represents the bioadhesive strength of the each formulation of buccal patches. The mean bioadhesive strength values were found to be 144.3, 149.34, 187.67, 176.28, 167.33, 132.64, 134.23, 167.35, 168.23 and 159.46 for F1 to
F10 respectively.

Force on adhesion (N) 1.40, 1.44, 1.82, 1.62, 1.75, 1.62, 1.42, 1.47, 1.76 and
1.12 (N) for F1 to F10 respectively. Bond strength (Nm^{-2}) 453.08, 432.12, 586.09, 543.63, 513.78, 421.12, 435.47, 564.65, 523.34 and 498.21 (Nm^{-2}) for F1 to F10 respectively.
Measurement of surface P^H :

Table no9.2 shows the result of surface ph values for each formulation. Thesevalues represent the mean of three replicate determinations. They were found to be with in the range of 6.3 to 6.6 for all formulations and were almost with in the rangeof salivary p^H i.e. 6.2 to 7.4. It represents the better patient acceptability.

Table .no. 6: Evaluation of Performance parameters of different mucoadhesivebuccal patches of Dimenhydrinate.

Formulation code	Performance parameters(Bio adhesive)		
	Bioadhesive strength(gms) ±S.D (n=3)	Force of adhesion(N) ±S.D(n=3)	Bond strength ±S.D (n=3) (kg/mm2)
F1	144.3± 2.64	1.40± 0.03	453.02± 5.34
F2	149.34± 2.13	1.44± 0.02	432.12± 3.65
F3	187.67± 0.78	1.82± 0.05	586.09± 5.23
F4	176.28± 0.98	1.62± 0.01	543.63± 1.86
F5	167.33± 1.34	1.75± 0.01	513.78± 4.33
F6	132.64± 3.67	1.62± 0.06	421.12± 6.98
F7	134.23± 2.87	1.42± 0.04	435.47± 5.32
F8	167.35± 1.74	1.47± 0.03	564.65± 6.90
F9	168.23± 1.53	1.76± 0.01	523.34± 3.23
F10	159.46± 1.13	1.12± 0.01	498.21± 4.98

Table No. 7: Evaluation of Performance parameters of different mucoadhesivebuccal patches of Dimenhydrinate.

Formulation code	Performance parameters(Bio adhesive)		
	Drug content(mgs) ±S.D (n=3)	Surface P^H ±S.D (n=3)	Invitro residence time (min)±S.D (n=3) (kg/mm2)
F1	3.73± 0.23	6.3± 0.54	320±10
F2	3.78± 0.13	6.4± 0.43	350±5
F3	3.71± 0.011	6.6± 0.57	490± 15
F4	3.80± 0.54	6.5± 0.43	420± 5
F5	3.75± 0.36	6.4± 0.57	450±10
F6	3.69± 0.45	6.4± 0.57	310±10
F7	3.68± 0.98	6.6± 0.23	300± 10
F8	3.76± 0.21	6.3± 0.45	421± 15
F9	3.73± 0.11	6.6± 0.34	480± 5
F10	3.78± 0.78	6.4± 0.23	430± 10

In vitro release study:

The in-vitro dissolution was studied in phosphate buffer p^H 6.8. The Invitro dissolution studies were carried out in triplicate and the results shown in the tables are

mean of the replicate values. The Invitro released data obtained for patches F1 to F10.

The results of Invitro dissolution studies obtained in these formulations were floated in 4 models of data treatments as follows

1. Cumulative percentage of drug released Vs time. (Zero order)
2. Log cumulative percentage of drug retained Vs time. (First order)
3. Cumulative percentage of drug released Vs square root of time. (Higuchi's plot)
4. Log cumulative percentage of drug released Vs log of time. (Peppa's plot)

Graph shows the plot of cumulative percentage of drug released as a function of time for different buccal patches. Cumulative percentage drug released as found to be 99.78% (8 hours), 99.58% (7 hours), 99.49% (10 hours), 100.17 (9 hours),

100.18% (9 hours), 97.15% (8 hours), 98.54% (8 hours), 100.75% (10 hours), 99.67%
(9 hours) and 100.6% (9 hours) for F1 to F10 respectively. The plot for cumulative percentage drug release verses time for all formulations

Stability study:
Stability studies of the prepared buccal patches were carried out, by storing formulations F5 at, room temperature and humidity and 40^0 C+ 2^0C/75%RH + 5% RH in humidity control oven for ninety days. Stability studies were carried out to predict the degradation that may occur over prolonged periods of storage at various temperatures and humidity for formulations F5 over a period of 90 days.
Kinetic study:

Table No.8: Invitro Drug Release of mucoadhesive buccal patches ofDimenhydrinateF1

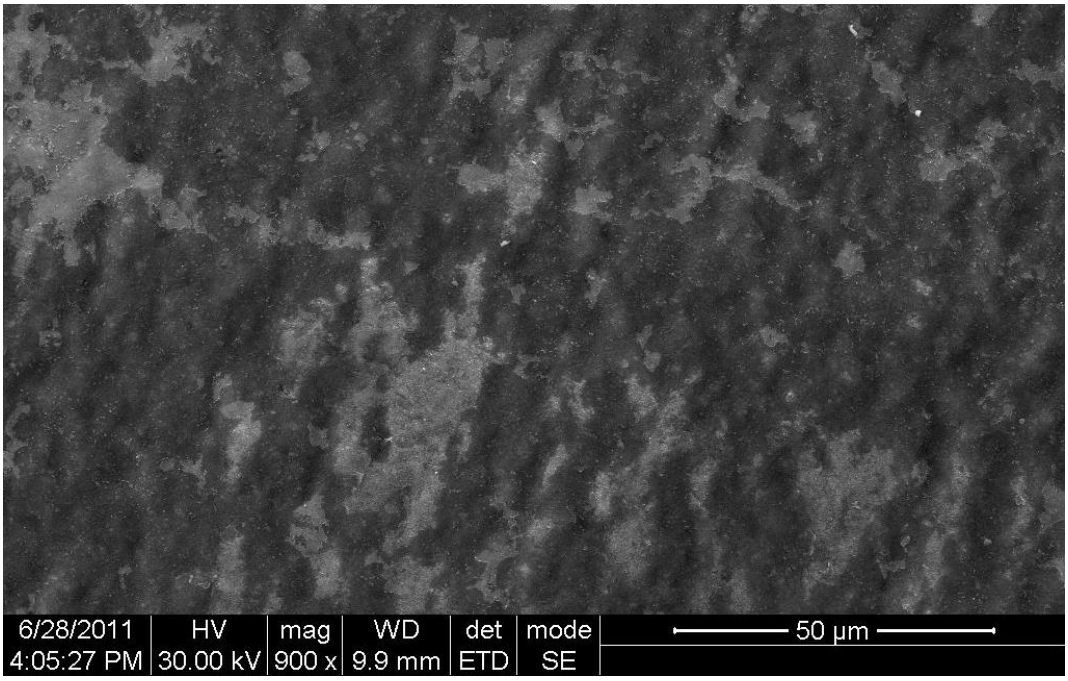
Time inhrs	Log time	SQ.RT of time	Abs (276nm)	Cum% release	Log cum% release
0	0.000	0.000	0.000	0.000	0.000
0.5	-0.301	0.707	0.016	11.59	1.064
1	0.000	1.000	0.027	19.67	1.294
2	0.301	1.414	0.047	34.36	1.536
3	0.477	1.732	0.061	44.85	1.651
4	0.602	2.000	0.085	62.68	1.797
5	0.698	2.236	0.101	74.89	1.874
6	0.778	2.449	0.112	83.59	1.922
7	0.845	2.645	0.123	92.37	1.965
8	0.903	2.828	0.132	99.78	1.999

Table. No. 9: Invitro Drug Release of mucoadhesive buccal patches ofDimenhydrinateF2

Time inhrs	Log time	SQ. RT of time	Abs (276nm)	Cum% release	Log cum% release
0	0.000	0.000	0.000	0.000	0.000
0.5	-0.301	0.707	0.023	16.4	1.214
1	0.000	1.000	0.045	32.25	1.508
2	0.301	1.414	0.065	46.83	1.670
3	0.477	1.732	0.087	62.98	1.799
4	0.602	2.000	0.105	76.44	1.883
5	0.698	2.236	0.112	82.18	1.914
6	0.778	2.449	0.128	94.39	1.974
7	0.845	2.645	0.134	99.58	1.998

FIGURE 3: SEM PHOTOGRAPH OF FORMULATION F5

A) SEM photograph of plain buccal patch



DISCUSSION:

Oral drug delivery system represents one of the frontier areas of controlled drug delivery system; such dosage forms are having a major advantage of patient compliance. A controlled release matrix dosage form is defined "as one for which the drug release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms.

Dimenhydrinate is H_1-antagonist used in the Treatment of nausea and vomiting caused by drug or motion sickness. The conventional doses release the entire drug in just few minutes and therefore the therapeutic concentrations are maintained for a short period of time generating a need for administration of another dose. Therefore, a sustained release formulation of Dimenhydrinate which would release the drug over a long period of time is beneficial.

In the present work efforts have been made to develop the controlled release Muccoadhesive buccal patches of Dimenhydrinate prepared by solvent casting technique using HPMC E15, HEC, PVA and PVP in different ratios to produce the therapeutic dose is needed to be maintained for long time.

PREFORMULATION PARAMETERS:

Determination of λ max of Dimenhydrinate:

On the basis of preliminary identification test it was concluded that the drug complied the preliminary identification. From the scanning of drug, it was concluded that the drug had λmax of 276 nm, which was equal to 276 nm as reported. Also, an IR spectrum was concordant with the reference spectrum of Dimenhydrinate.

Preparation of standard calibration curve of Dimenhydrinate:

From the standard curve of Dimenhydrinate, it was observed that the drug obeys beer's law in concentration range of 1-10 µg/ml in Distilled water. The linear Regression equation generated was used for the calculationof amount of drug.

Determination of IR spectrum of Dimenhydrinate:

Physical mixture of drug and polymer was characterized by FT-IR spectral analysis for any physical as well as chemical alteration of the drug characteristics. From the results, it was concluded

that there was no interference in the functional group as the principle peaks of the Dimenhydrinate were found to be unaltered in the drug-polymer physical mixture, indicating they were compatible chemically.

Drug excipient compatibility studies:
Drug-Excipient compatibility studies form an important part of Preformulation studies for the determination of interaction between drug and excipient. It is determined after storage of specific time period by using suitable analytical techniques and the results are indicating that there is no interaction between drug andexcipients.

FORMULATION DESIGN:
Formulation of the controlled release mucoadhesive buccal patches of Dimenhydrinate:
Formulations of Muccoadhesive buccal patches were prepared with different polymers such as HPMC E15, HEC, PVA and PVP in different Ratios and proportions by Solvent casting technique. The prepared Muccoadhesive patches were then evaluated for various physico-chemical tests like thickness, folding endurance, weight variation, water uptake, bioadhesive strength, drug content uniformity, surfacep^H, Mechanical strength, Scanning electron microscopy (SEM), In-vitro release study, Invitro residence time, Ex-vivo drug release study, Stability study and Kinetic study.

EVALUATION PARAMETERS:
Physical properties:
Thickness of patch:
The thickness of the prepared buccal patches of each formulation was determined with in the range of 0.23- 0.26mm.

Folding endurance:
The folding endurance of each formulation was determined with in the range of 302 to 318. It revealed that good flexibility of patch.

Mechanical strength:
Three patches of each formulation were evaluated and mean values are recorded in table no.9.1. The values were found to be in the range of 5.28 to 12.94kg/mm^2. The values revealed that the patches were having good mechanical strength.

Water uptake study:
Water uptake of all buccal patches containing Dimenhydrinate is given in table no.9.1. The swelling of patch was changes with respect to polymer ratios. The values were found to be with in the range of 1.93 to 2.93.it was maximum for F3 i.e.

It is revealed that swelling nature of polymer parameters:
Content uniformity of active ingredient:
Table no.9.2 shows the result of drug content uniformity in each formulation. Three replicates of each test were carried out. The mean drug content was found to bein the range of 3.68 to 3.8 for (each patch size 10mm diameter) the prepared buccal patch formulations. It is indicating the uniform distribution of drug in polymer matrix.

Measurement of bioadhesive strength:
An effective buccal mucosal device must maintain an intimate contact with mucus layer overlying the epithelial tissue. This parameter very important to successful utilization of these dosage forms. Hence in-vitro evaluation of buccal patches was carried out using porcine gastric mucosa. This gives the indirect measurement of bioadhesive strength in grams.

The maximum bioadhesive strength and force of adhesion was recorded for the formulation F3 and the values were 187.67 and 1.82 respectively. The Invitro residence time was recorded and the values were changing with different ratios of polymers and the maximum for F3 about 490 mins.

Measurement of surface P^H :
They were found to be with in the range of 6.3 to 6.6 for all formulations andwere almost with in the range of salivary p^H i.e. 6.2 to 7.4. There was no considerable difference in surface p^H of patches. It represents the better patient acceptability.

In vitro release study:
The in-vitro dissolution was studied in phosphate buffer p^H 6.8. The Invitro dissolution studies were carried out in triplicate and the results shown in the tables are mean of the replicate values. The Invitro released data obtained for patches F1 to F10 are tabulated in table no.10 to 19 respectively. The maximum release was observed in F3 formulation, it was up to 10 hours. The release is due to the uniform and proper mixing of drug and polymers which enables the drug to release in steady state manner.

Criteria for optimization:
The formulation F3 is optimized on the basis of Invitro drug release, swelling index, long Invitro

residence time and good bioadhesive strength. The Ex-vivo release studies were performed by using 7.4 P^H saline phosphate buffer for formulation F3 by using porcine buccal mucosa as a model membrane and it was shown that good drug permeability across the membrane above 10 hours.

Stability study:
Stability studies of the prepared buccal patches were carried out, by storing formulations F3 at, room temperature and humidity and 40^0 C±2^0C/ 75%RH ± 5% RH in humidity control oven for ninety days. Stability studies were carried out to predict the degradation that may occur over prolonged periods of storage at various temperatures and humidity for formulations F3 over a period of 90 days. The results of the stability studies, which were conducted for 90 days, are shown in table no.24. The result obtained showed a slight decrease in, in vitro release of formulations F3 as compared to the fresh formulations F3. The shelf life of the fabricated device was calculated based on these parameters.

Kinetic study:
To study the drug release kinetics, data obtained from In-Vitro drug release studies are plotted in various kinetic models. The curve fitting results of the release rate profile of the designed formulations gave an idea on the mechanism of drug release.
Based on the "n" values are ranging from 0.745-0.893 for all the formulations formulation, the drug release was found to follow Anomalous (non-Fickian) diffusion. This value indicates a coupling of the diffusion and erosion mechanism (Anomalous diffusion) and indicates that the drug release was controlled by more than one process. Also, the drug release mechanism was best explained by zero order, as the plots showed the highest linearity (r^2 = 0.971), as the drug release was best fitted in zero order kinetics, it indicated that the rate of drug release is concentration independent.
Formulation F3 showed good Bioadhesive strength and a controlled drug release and also shown good result for all other parameters when compared with all other formulations. Hence formulation F3 is considered to be the optimized formulation. Stability studies were carried out for F3 formulation they had showed good stability when stored at accelerated stability state as per the ICH guideline and the values were with in a permissible limits.
It was observed that Formulations F3 retained the drug release up to 24 hrs. All formulations were subjected for four different models viz. Zero order, First order, Higuchi matrix and Peppas model equations and all the formulations best fit in to the Peppas model by giving the values of diffusional exponent (n) in the range of 0.6-0.9that indicate the formulation had release the drug by diffusion followed by erosion mechanism.

It was revealed that polymer ratios had significant influence on drug release. Thus conclusion can be made that stable dosage form can be developed for Dimenhydrinate for controlled release by buccal patches.

CONCLUSION:

In the present study, an attempt has been done to develop a novel muccoadhesive drug delivery system in the form of the buccal patches for the release of Dimenhydrinate in a bidirectional manner, to maintain constant therapeutic levels of the drug for long time.
Buccal formulations of Dimenhydrinate in the form of muccoadhesive patches were developed to a satisfactory level in term of drug release, bioadhesive strength, content uniformity, percentage water uptake, surface P^H, thickness and mechanical strength.
Although all buccal patches exhibited satisfactory results, best results were obtained with optimized formulation F3 containing HPMC and HEC in 1:3 ratios. Invitro dissolution studies of the optimized formulation showed that the percentage cumulative drug release about the release of Dimenhydrinate from the patches in the present work appeared to occur due to diffusion and erosion mechanism. The releasepattern was found to be non-Fickian.
The above study concluded that the possibility of the making of mucoadhesive drug delivery system for Dimenhydrinate which will be more efficacious and acceptable than conventional drug delivery of Dimenhydrinate and also having satisfactory controlled release profile which may provide an increased therapeutic efficacy.

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