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FORMULATION AND EVALUATION OF CHITOSAN BASED BUCCAL PATCH OF GRANISETRON HYDROCHLORIDE

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ABSTRACT

Granisetron hydrochloride is most commonly used as an antiemetic agent in treatment associated with cancer chemotherapy induced nausea and vomiting. If the dosage form is designed in sustain release it provide more advantage for the antiemetic therapy. The purpose of this research was to study mucoadhesive buccal patches of Granisetron hydrochloride using the bioadhesive polymers chitosan and sodium alginate. Patches containing chitosan in 1.5%w/v and sodium alginate 2%w/v had maximum percentage of *in vitro* drug release and *ex vivo* drug permeation upto 8 hr. The swelling index was proportional to chitosan and sodium alginate content. The surface pH of all patches was found to be satisfactory (7.0 ± 1.5), close to neutral pH; hence, buccal cavity irritation will not be a problem with these patches. The mechanism of drug release was found to be Higuchi (matrix). The formulation F6 was optimized based on good bioadhesive strength (326.96±0.99 N/M^2) and sustained *in vitro* drug release (95.81% ± 3.21% for 8 hr), *ex vivo* permeation (96.59% ± 3.69% for 8 hr).

INTRODUCTION: There is need to develop a dosage form that bypasses first pass metabolism and GI degradation. Oral cavity provide route for the administration of therapeutic agent for local as well as systemic delivery, so that first pass metabolism and GI degradation can be avoided. The buccal route was chosen because of its good accessibility, robustness of epithelium, facile removal of the dosage form, relatively low enzymatic activity and natural clearance mechanism for elimination of the drug from buccal area, satisfactory patient acceptance and avoiding the hepatic first pass metabolism [1].

GRA.HCl is rapidly absorbed from the GIT, but later it is subjected to extensive first pass metabolism. In healthy volunteer, half-life of the drug is reported to be about 3-4 hr.

Therefore, current GRA.HCl treatment generally involve oral dose of 1-2 mg, one hour before start of chemotherapy treatment, then 2 mg daily in 1-2 divided doses upto 4 days. Also a single 3 mg IV dose of GRA can be administered, repeated if necessary with a maximum daily dose of 9 mg [2, 3]. But there are some limitations for GRA.HCl when given by oral route.

If patient started vomiting, oral route cannot be used and some alternative routes of administration like parenteral, transdermal, rectal or buccal administration are needed. Amongst all, parenteral require skillful person as well as hospitalization. When we consider rectal route, it take lag time to show antiemetic action and is quite unacceptable route by the patient.

But if we consider buccal route, it may provide advantages of other routes.

Literature survey indicated that GRA.HCl can be a good candidate for the buccal drug delivery system and also no work is reported for the development and evaluation of GRA.HCl as a buccal patch. Hence, we tried to develop buccal drug delivery system containing GRA.HCl. Being a non-toxic, biocompatible and biodegradable polymer, chitosan has been widely used for pharmaceutical and medical applications. Chitosan was considered as a good bioadhesive material for the present study [4, 5.] Hence development of buccal patch of GRA.HCl providing immediate onset of action followed by sustained release of drug so as to have effective antiemetic therapy for longer period of time is the need of an hour.

In this study attempt was made to develop a GRA. HCl buccal patch which will initially release drug immediately followed by prolonged release, thus avoiding presystemic metabolism and overcoming the limitation of oral route.

MATERIALS AND METHODS

Materials: GRA.HCl, a gift sample from Wockhardt ltd. Aurangabad. Chitosan, gift sample from V. Kumar and sons Aurangabad. Sodium alginate, propylene glycol purchase from Dipa chemicals Aurangabad.

Preparation of Buccal Patches: The mucoadhesive buccal patches were prepared by solvent casting method in different concentration of chitosan as given in **Table 1**.

TABLE 1: COMPOSITION OF BUCCAL PATCHES OF GRA.HCl

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Chitosan in %w/v	1	1	1	1.5	1.5	1.5	2	2	**2**
NA-alginate in %w/v	1	1.5	2	1	1.5	2	1	1.5	**2**
Drug in mg	2	2	2	2	2	2	2	2	**2**
Propylene glycol in %v/v	**5**	**5**	**5**	**5**	**5**	**5**	**5**	**5**	**5**

GRA HCl indicates granisetron hydrochloride; Na-alginate sodium alginate

The polymeric solution of chitosan was prepared using 1.5%v/v acetic acid in distilled water with occasional stirring for 48 hr. The resultant viscous chitosan solution was filtered through nylon gauze to remove cell debris and suspended particles. Propylene glycol was added as a plasticizer under constant stirring. The resultant solution was left overnight at room temperature to ensure clear bubble free solution.

Then the solution was poured into the mould. The amount of drug required in the mould was calculated. The amount of the drug required in the mould is mainly depends on the surface area of the mould [6, 7]. The mould was kept at level position and covered by inverted funnel to controlled evaporation of the solvent at room temperature till dried flexible patch was formed. Dried patch was carefully removed, checked for any imperfection and air bubble and cut into patch of $1cm^2$. The patch containing GRA.HCl was packed in aluminium foil and stored in air tight container to maintain integrity and elasticity of the patch.

Evaluation of Factorial Batches [8, 9]:

Uniformity in weight: Uniformity in weight of patch was determined by taking weight of six patches from every batch and weighed individually on weighing balance.

Thickness: The thickness of three randomly selected buccal patches from every batch was determined using a digital vernier calliper (STAINLESS HARDEND).

Surface pH study: A combined glass electrode was used for this purpose. The buccal patch was allowed to swell by keeping it in contact with 1ml of distilled water for 1 hr at room temperature. The pH was measured by bringing the electrode in contact with the surface of the patch and allowing it to equilibrate for 1min. The experiment was performed in triplicate, and average values were reported.

Content uniformity: Drug content uniformity was determined by dissolving the buccal patch from each batch by homogenization in 100ml of a

phosphate buffer (pH 6.8) for 6 hr under occasional shaking. 5ml solution was taken and diluted with phosphate buffer pH 6.8 up to 20ml and the resulting solution was filtered through a 0.45µm syringe filter. The drug content was then determined after proper dilution at 302nm using a UV Spectro-photometer.

Folding endurance: Folding endurance of the patch was determined by repeatedly folding one patch at the same place till it breaks or folded upto 300 times manually. The number of times of patch could be folded at the same place without breaking gave the value of the folding endurance. This test was done on randomly selected three patches from each batch.

Swelling index study: A patch from every batch was weighed on a preweighed cover slip. It was kept in a petridish and 10ml of phosphate buffer, pH 6.8 was added. After 1 hr, the cover slip was removed and weighed. The difference in the weights gives the weight increase due to absorption of water and swelling of patch.

$$\% S = (Xt - Xo / Xo) \times 100$$

Where, Xt is the weight or area of the swollen patch after time t and Xo is the original patch weight or area at zero time.

Determination of *in vitro* Residence Time: The *in vitro* residence time was determined using a USP disintegration apparatus. The disintegration medium was composed of 800ml pH 6.8 PB maintained at 37 ± 0.5°C. A goat buccal mucosa was vertically attached to the apparatus. The mucoadhesive patch was hydrated from one surface using 15µl pH 6.8 PB and then the hydrated surface was brought into contact with the mucosal membrane.

The glass slab was vertically fixed to the apparatus and allowed to move up and down so that the patch was completely immersed in the buffer solution at the lowest point and was out at the highest point. The time necessary for complete erosion or detachment of the patch of each batch from the mucosal surface was recorded.

Measurement of Mucoadhesive Strength: Fresh goat buccal mucosa was obtained from a local slaughter house and used within 2 hr of slaughter. The mucosal membrane was separated by removing the underlying fat and loose tissues. The membrane was washed with distilled water and then with pH 6.8 PB as moistening fluid. Briefly, buccal mucosa section was fixed on the plane surface of glass slide attached (with adhesive tape) to bottom of smaller beaker, kept inverted in 500ml beaker attached to the bigger beaker. Phosphate buffer pH 6.8 was added to the beaker up to the upper surface of inverted beaker with buccal mucosa. The buccal patch was stuck to the lower side of the upper clamp with cyanoacrylate adhesive.

The exposed patch surface was moistened with 15µl of pH 6.8 PB and left for 30s for initial hydration and swelling. Then the platform was slowly raised until the patch surface came in contact with mucosa. Two sides of the balance were made equal before study. After a preload (50g) time of 2min, water was added to the polypropylene bottle present in another arm, until the patch was detached from the buccal mucosa. The water collected in the bottle was measured and expressed as weight (g) required for the detachment. The force measurement was repeated 3 times for each formulation. The following parameters were calculated from the bioadhesive strength:

Force of adhesion (N) =

(Bioadhesive strength (g) × 9.81)/1000

Bond strength (Nm^{-2}) =

Force of adhesion / Disk surface area

Moisture absorption study: The moisture absorption study gives an indication about the relative moisture absorption capacities of polymers and an idea whether the formulation maintains its integrity after absorption of moisture, 5%w/v agar in distilled water, in hot condition, was transferred into petri plates and it was allowed to solidify. Six patches of each formulation were selected and weighed. The patches were placed in desiccator overnight prior to the study to remove moisture if any and laminated on one side

with water impermeable backing membrane. They were placed on the surface of the agar and incubated at 37°C for 1 hr in incubator. The patches were removed and weighed again. The percentage of moisture absorbed can be calculated using the formula:

% Moisture absorbed =

Final weight - Initial weight/ Initial weight × 100

Surface Study of the Patch: Surface of the patch was studied by optical microscopy with digital camera (Olympus).

***Ex vivo* Buccal Permeation study:** The test was carried out using goat buccal mucosa. The buccal epithelium was used within 2 hr upon removal. The Keshary chain diffusion cell was used to permeation studies, it consists of two compartments, one is donor compartment and another is receptor compartment. The assembly of diffusion study is shown in **Fig. 1**.

FIG. 1: ASSEMBLY OF DIFFUSION CELL

The receptor compartment was covered with water jacket to maintain temperature 37°C. The receptor chamber was filled with pH 6.8 PB and buccal epithelium was mounted over it. Buccal mucosa was allowed to stabilize for the period of 1 hr. After stabilization, patch was kept on epithelium and periodically (for 8 hr) samples were withdrawn and maintained sink condition. The aliquot were analyzed spectrophotometrically at 302nm. The drug permeation was correlated with cumulative drug released.

***In vitro* Release Study:** The USP dissolution apparatus 2 (paddle) was used to study the drug release from buccal patches. The dissolution medium consisted of 500ml of pH 6.8 PB. The release was performed at 37 ± 0.5°C, at a rotation speed of 50rpm. One side of the buccal patch was attached to a glass disk with instant adhesive (cyanoacrylate). The disk was put in the bottom of the dissolution vessel so that the patch remained on the upper side of the disk. Samples (5ml) were withdrawn by using calibrated pipette at pre-determined time (1 hr) intervals and replaced with fresh medium. The samples were filtered through 0.45µm syringe filter with appropriate dilutions with pH 6.8 PB and were assayed spectrophotometrically at 302nm.

Kinetics of drug release: Curve fitting and model fitting: The dissolution profile of all the batches were fitted to various mathematical models for describing the release mechanism for buccal patches; Kosmeyer-Peppas, zero order and Higuchi release model to ascertain the kinetic modelling of drug release by using a (PCP Disso V 2.08) software and the model with the higher correlation coefficient was considered to be the best fit model.

Statistical Analysis: A 3^2 full factorial design was selected and 2 factors were evaluated at 3 levels, respectively. The statistical treatment and inter-pretation of data was done by Stat Ease Design expert 8.05 software. The analysis of variance (ANOVA) was calculated. The data were subjected to 3D response surface methodology to study the interaction of independent variables.

RESULTS AND DISCUSSION: Chitosan and Na-alginate were selected as the bioadhesive polymers because of their excellent bioadhesive properties.

In the preparation of the patch concentration, plasticizer play an important role in flexibility and formation of the patch. Propylene glycol is used as a plasticizer. Hence, from the result given in **Table 2.**

At room temperature patches were formed but this procedure required 2-3 days. So drying of the patch was carried out in the hot air oven at 40°C. Time is important factor for formation of the patch. The optimization of drying time is shown in **Table 3.**

If the patch was dried for less than 8 hr then it contained some amount of moisture that looses physical properties of the patch and if patch was over heated then patch loses its integrity, breaks easily. Hence at 8 hr drying, patch was found with optimized moisture and good physical properties. The various parameters of prepared patches were evaluated as per prescribed method. Evaluation parameters are shown in **Table 4**.

TABLE 2: OPTIMIZATION OF PLASTICIZER

Conc. of chitosan (%w/v)	Conc. of plasticizer (%v/v)	Result
1%	2%	Thin patch breakable doesn't show flexibility
1%	3%	Thin patch breakable but show some flexibility
1%	5%	Thin patch having flexibility and it does not break easily
1%	7%	Patch was not formed
1.5%	2%	Patch having some thickness but didn't show flexibility and breakable
1.5%	3%	Patch having some thickness but didn't show flexibility but it does not break easily
1.5%	5%	Patch having some thickness having flexibility and it does not break easily
1.5%	7%	Patch was not formed
2%	2%	Thick patch but didn't show flexibility and breakable
2%	3%	Thick patch but didn't show flexibility but it does not break easily
2%	5%	Thick patch having flexibility and it does not break easily
2%	7%	Patch was not formed

5%v/v plasticizer showed optimizes patch physical properties i.e. patch with good flexibility.

TABLE 3: OPTIMIZATION OF DRYING TIME AT 40^{o}C

Time	wt of 1	wt of 2	wt of 3
0 hr	127.58g	127.52g	124.60g
2 hr	125.85g	118.25g	119.66g
4 hr	119.10g	117.48g	110.38g
6 hr	116.28g	114.45g	108.54g
8 hr	112.293g	111.50g	108.48g

TABLE 4: EVALUATION PARAMETER OF FORMULATION

Parameter	F1	F2	F3	F4	F5	F6	F7	F8	F9
Wt. variation (mg)	28.93±0.901	32.76±0.802	37.16±0.939	32.89±0.912	45.005±0.835	45.90±0.877	36.08±0.723	44.3±0.593	55.35±0.559
Thickness (µm)	55	52	56	55	56	55	55	54	56
Surface pH	5.54	6.06	6.14	6.19	6.23	6.09	6.35	6.43	6.51
Content uniformity (%)	94.76	95.65	96.35	94.67	98.12	98.90	97.56	95.35	97.45
Folding endurance	>300	>300	>300	>300	>300	>300	>300	>300	>300
Swelling index (%)	33.33	40.62	65.78	35.29	42.85	79.16	35.13	64.44	86.53
Mucoadhesion time (hr)	2.28	2.23	1.67	3.4	3.41	3.21	2.66	2.4	2.13
Bond strength (N/M^2)	186.4	176.86	164.8	350.5	344.93	326.96	380.96	358.36	341.4
%Moisture absorbance	109.15	121.45	135.35	145.35	155.35	167.35	174	178.34	189.56

The average weight of buccal patches (F1 to F9) was determined. Result indicated that there was good uniformity of weight in patch. The average weight of patches (F1 – F9) were found to be 28.93±0.901 mg, 32.76±0.802 mg, 37.16±0.939 mg, 32.89±0.912 mg, 45.005±0.835 mg, 45.90±0.877 mg, 36.08±0.723 mg, 44.3±0.593 mg, 55.35±0.559 mg. The surface pH of buccal patches was found within the range. The pH of patch was found to be in the range of 5.5 to 6.5. Folding of the patches was done for about more than 300 times at same point. There was no breaking of the patch found.

The swelling index of all patches were good. From the study; it was observed that the rate of swelling has direct correlation with amount of chitosan present Sodium alginate polymer is hydrophilic in nature, due to this patches detaches from the mucosa. Among the all formulation F5 shows highest mucoadhesion time. Concentration of mucoadhesive polymer increased there was increase in mucoadhesive strength of the patch. But due to presence of the hydrophilic polymer the mucoadhesive strength set decreased. The F7 formulation showed highest mucoadhesive strength 380.976NM^{-2}. Surface study of the patches showed that there are the uniformity in thickness within a patch and there were no air entrapment in the patch. Surface study showed in the **Fig. 2**.

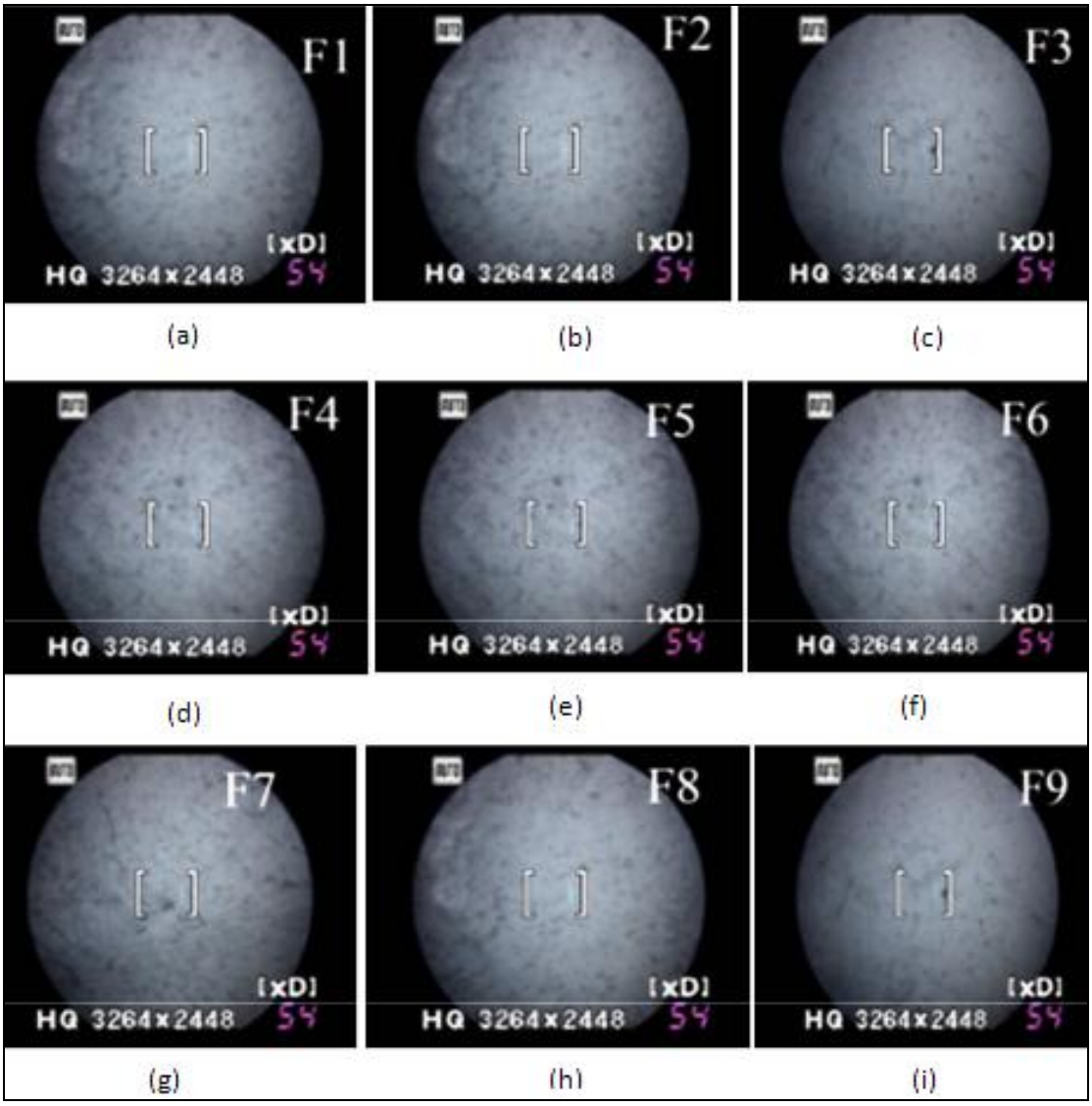

FIG. 2: SURFACE PROPERTIES OF FACTORIAL BUCCAL PATCHES

Ex vivo permeation through the goat buccal mucosa, F6 batch showed drug release upto 96.59%. F1 to F3 showed maximum drug release at 7 hr. F4 to F9 exhibited drug release upto 8 hr. As the concentration of the chitosan increases the drug release also get retarded. As the concentration of the hydrophilic polymer that is sodium alginate was increased there is increase in the drug release. F9 batch however shows decrease in the permeation. This may be attributed to the fact that increase in hydrophilic polymer conc. i.e. sodium alginate, because of its low bioadhesive properties may get detached from the mucosal surface and results in less permeation in addition to the fact that increase in chitosan concentration causes increase in swelling and viscosity resulting in increase in tortuosity. Graphical representation of *ex vivo* permeation studies are shown in **Fig. 3, Fig. 4, Fig. 5**.

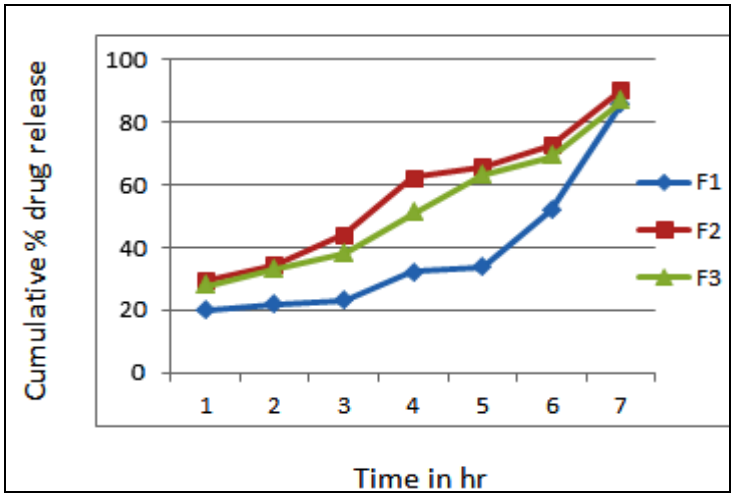

FIG. 3: *EX VIVO* DRUG RELEASE OF FORMULATION F1, F2, F3

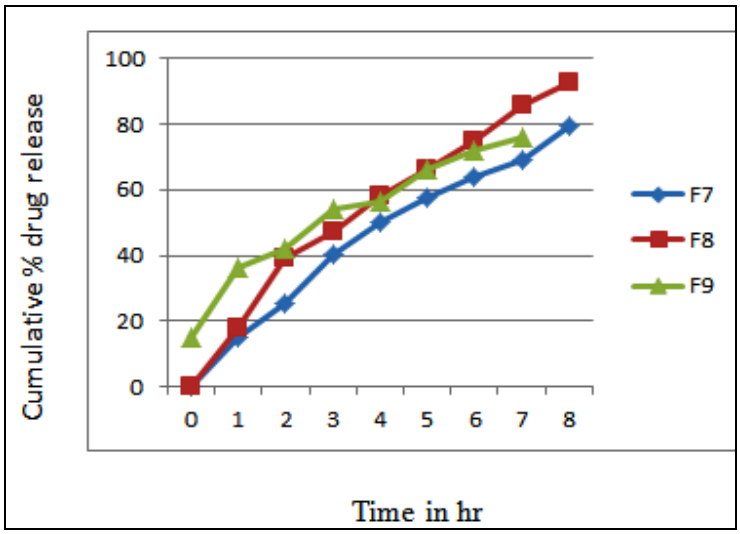

FIG. 4: *EX VIVO* DRUG RELEASE OF FORMULATION F4, F5, F6

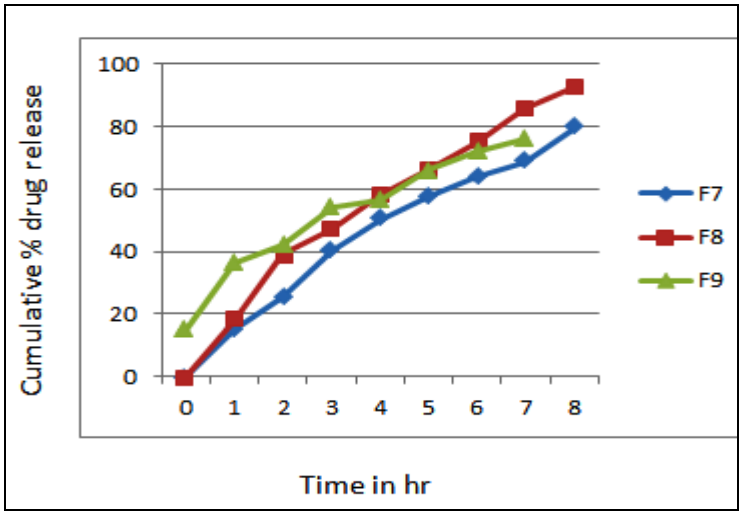

FIG. 5: *EX VIVO* DRUG RELEASE OF FORMULATION F7, F8, F9

It was found that during dissolution there is sudden release of drug maximum upto 30% in 1 hr. This is due to the fact that the drug is hydrophilic in nature as well as highly soluble in dissolution medium.

If the amount of polymer is increased in order to prevent sudden release of drug in first hour. The F3 have shown maximum drug release in first hour. Increased in the concentration of the chitosan, release of the drug get retarded due to high polymeric content. But as the concentration of the sodium alginate which is hydrophilic in nature increases, it enhanced the drug release.

F1 shows drug release upto 91.61% in 7 hr and this may be due to less concentration of chitosan present in patch. F2 showed drug release up to 92.21% and F3 have shown drug release upto 94.81% in 7 hr. These increased in cumulative drug release may take place due to increase in the concentration of hydrophilic polymer, sodium alginate. F4, F5 and F6 formulation showed drug release 91.62%, 93.65% and 95.81% in 8 hr respectively.

F7, F8 and F9 showed drug release 83.01%, 88.21%, and 91.01% in 8 hr respectively. These decreased in drug release is due to increased thickness of the gel layer formed by mucoadhesive polymer, chitosan with increase path length and tortuosity.

The gel layer is formed on contact with dissolution medium which lead to retardation of drug from the patch. The $T_{50\%}$ value for F1 to F9 lies in between 3 to 5 hr. *In vitro* drug release studies are shown in Fig. 6, Fig. 7, and Fig. 8 .

The various kinetic models were applied as stated earlier in order to interpret the drug release pattern. The kinetics models followed by all formulation from F1 to F9 are shown in **Table 5**.

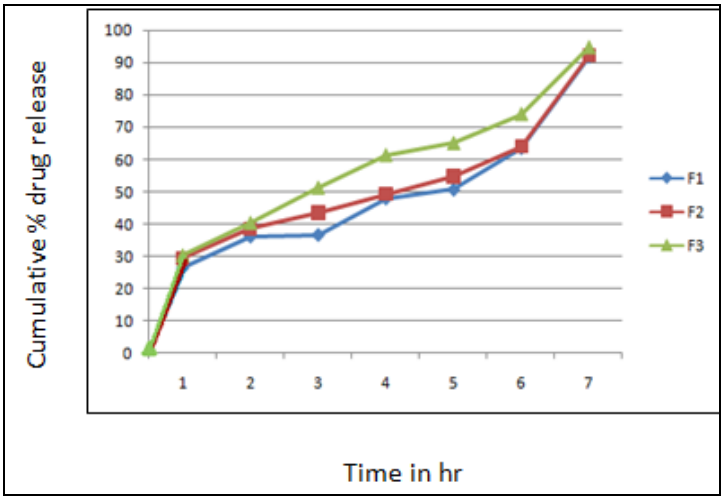

FIG. 6: DRUG RELEASE PROFILE OF F1 TO F3

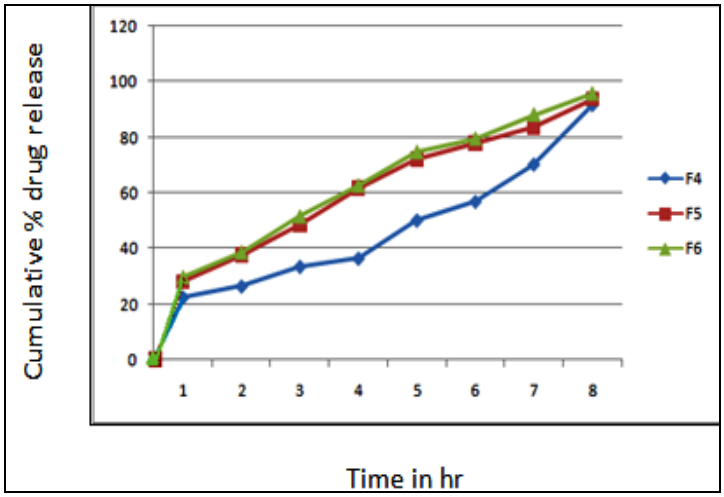

FIG. 7: DRUG RELEASE PROFILE OF F4 TO F6

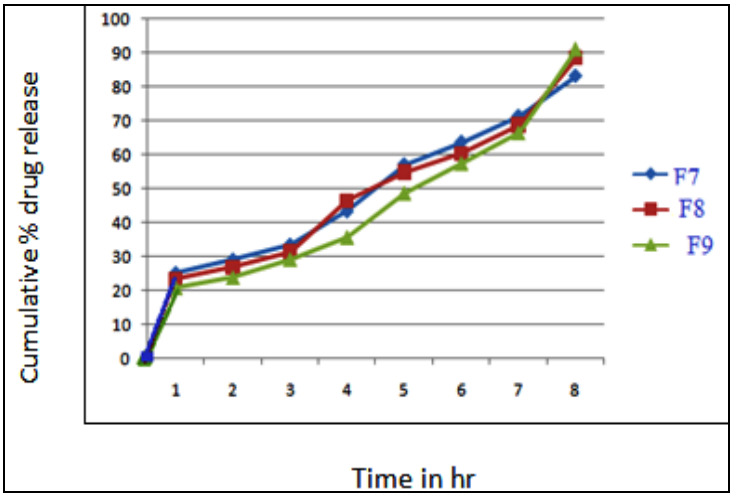

FIG. 8: DRUG RELEASE PROFILE OF F7 TO F9

TABLE 5 : DISSOLUTION MODELS

Formulation code	Dissolution models (r^2 values)					
	Zero order	First order	Matrix model (Higuchi)	Kosermeyer - peppas	Hixon crowell	Best fit model
F1	0.8913	0.8945	0.9756	0.8947	0.8754	Matrix (Higuchi)
F2	0.8998	0.8978	0.9837	0.9386	0.8967	Matrix (Higuchi)
F3	0.8856	0.8742	0.9609	0.9513	0.8575	Matrix (Higuchi)
F4	0.8546	0.7056	0.9701	0.9457	0.9324	Matrix (Higuchi)
F5	0.8976	0.8178	0.9834	0.8936	0.9567	Matrix (Higuchi)
F6	**0.9076**	**0.9834**	**0.9956**	**0.9812**	**0.9754**	**Matrix (Higuchi)**
F7	0.8802	0.9245	0.9178	0.8754	0.9799	Matrix (Higuchi)
F8	0.8923	0.9380	0.9467	0.8753	0.9568	Matrix (Higuchi)
F9	0.7934	0.9421	0.8967	0.9598	0.8756	Matrix (Higuchi)

The results indicate that all the formulation followed Matrix (Higuchi) model. According to this model the drug release is directly proportional to the square root of time. The n value for all formulation was found to close to 0.5. *In vitro* studies were performed to get idea about the drug release from the dosage form in the physiological condition and kinetics of drug release. Depending upon the drug release from the dosage form, one can predict the *in vivo* drug release from the same dosage form. Various parameters of Kosmeyer Peppas are shown in **Table 6**.

TABLE 6: PARAMETERS FOR KOSMEYER PEPPAS EQUATION

	F1	F2	F3	F4	F5	F6	F7	F8	F9
N	0.4216	0.4785	0.4867	0.4976	0.4186	0.4167	0.4654	0.4567	0.4327
K	35.24	33.37	35.65	35.46	33.98	30.91	35.77	32.89	34.02

The 3^2 full factorial designs was applied to study the effect of independent variables such as chitosan % (X1) and sodium alginate % (X2) on dependent variables such as mucoadhesion strength, Muco-adhesion time and % drug release at 8h. The response data was analysed by using Stat Ease Design Expert 8.0.5 software. This gives statistical analysis of data. The summary of statistical design and summary of response are given in **Table 7 and 8**. The result of statistical data is reported in **Table 9**.

TABLE 7: SUMMARY OF STATISTICAL DESIGN

Factor	Name	Units	Type	Low Actual	High Actual	Low Coded	High Coded
1	Chitosan	%	Numerical	1	2	-1	+1
2	Sod. alginate	%	Numerical	1	2	-1	+1

TABLE 8: SUMMARY RESPONSES

Response	Name	Observations	Analysis	Minimum	Maximum	Mean
Y1	Mucoadhesion strength	9	Polynomial	164.80	380.96	293.35
Y2	% Drug release at 8 hr	9	Polynomial	83.01	95.81	91.32
Y3	Mucoadhesion residence time	9	Polynomial	1.67	3.41	2.603

TABLE 9: ANOVA STUDY-P-VALUE

Response	R^2	P<0.05 model	Model significant/non significant
Mucoadhesive strength	0.9993	0.0001	Significant
%Drug release at 8hr	0.9806	0.0090	Significant
Mucoadhesion time	0.9789	0.0102	Significant

The response surface method shows the interaction plot of independent variables. The response surface plots for Y1, Y2 Y3 are shown in **Fig. 9, 10 and 11** respectively.

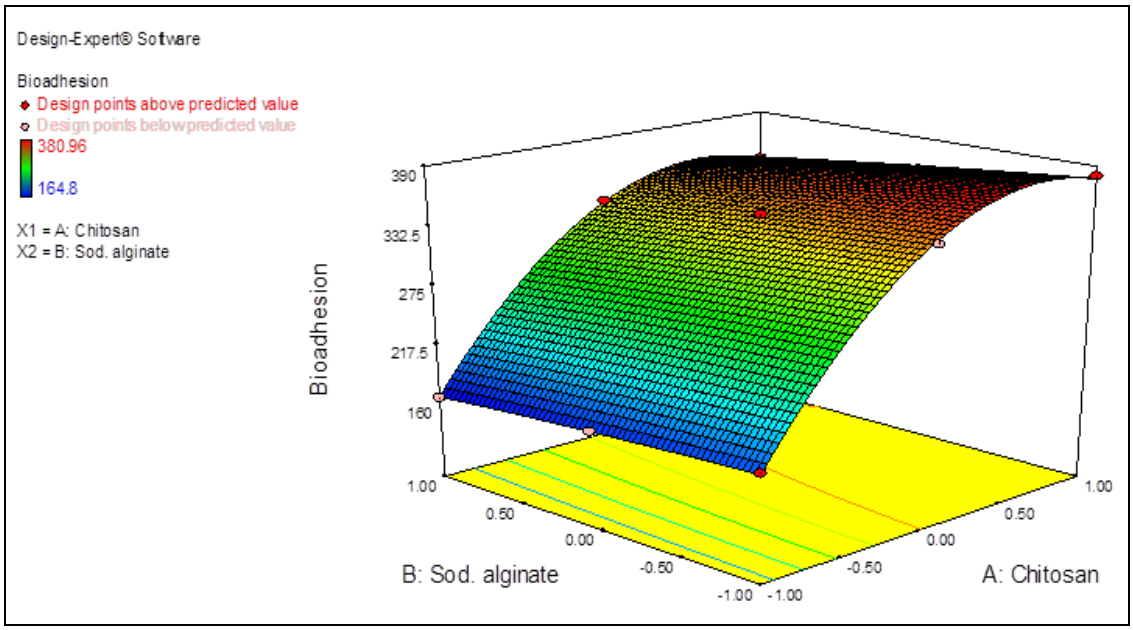

FIG. 9: RESPONSE SURFACE PLOT OF MUCOADHESIVE STRENGTH

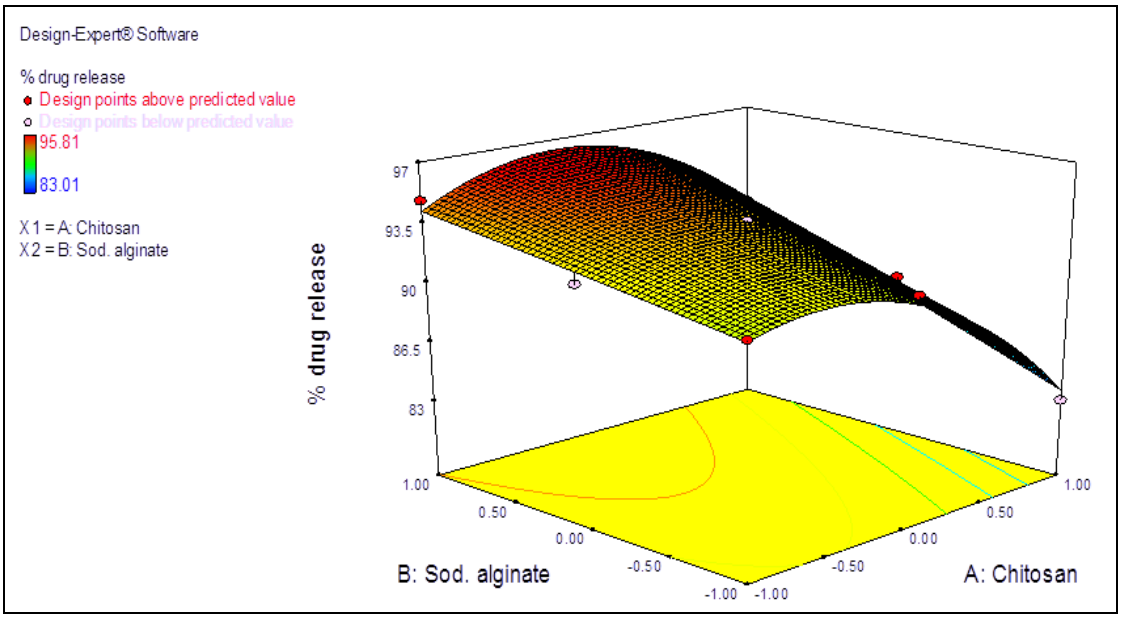

FIG. 10: RESPONSE SURFACE PLOT OF % DRUG RELEASE AT 8 hr

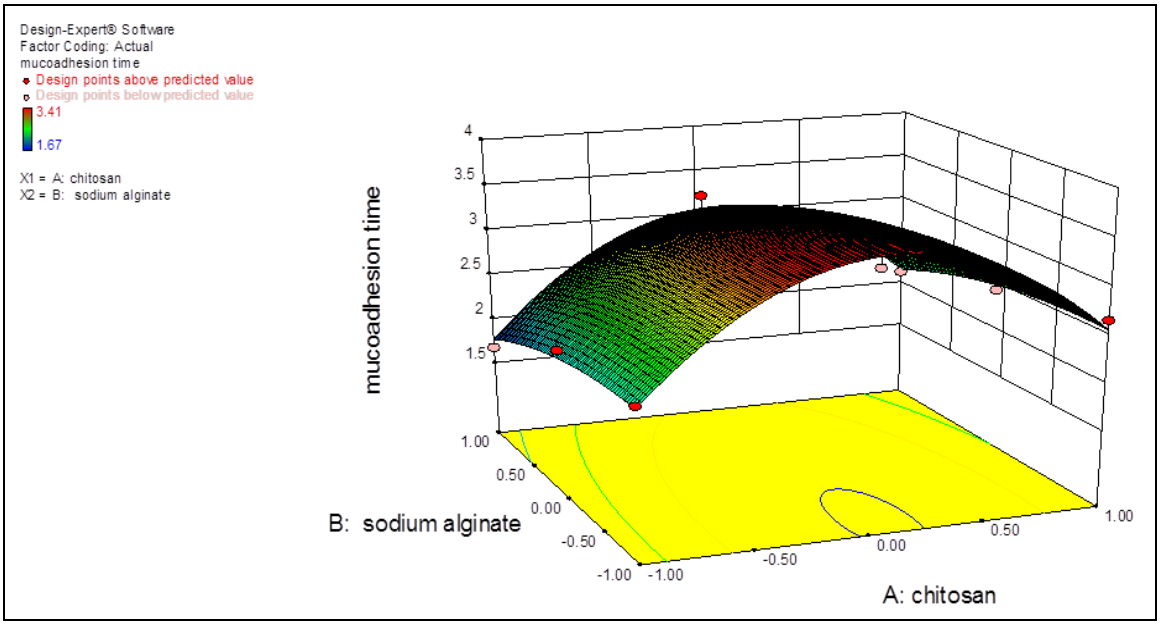

FIG: 11: RESPONSE SURFACE PLOT OF MUCOADHESION TIME

The effect of interaction of these independent factors on the drug release at various intervals can be studied using the result of statistical analysis Fig. 9, 10 and 11 represent the response surface plots. The mucoadhesive strength was increased with increasing amount of the chitosan.

Chitosan base has good bioadhesion properties in appropriate concentration, and good bond strength forming capacity with mucin. But as the concentration of sodium alginate increases, the bioadhesive strength was found very less, may be due to hydrophilic natures which loosen the bond strength with mucosal area.

So patch might be detached as it absorbs water molecule. Fig. 10 shows drug release in 8h. is decreases as the amount of the chitosan increases. Sodium alginate was used to increases the drug release from the patch. An optimum amount of the hydrophilic chitosan and sodium alginate in F6 shows highest drug release at 8h.

Fig. 11 shows the response of the mucoadhesion residence time in hours in that case as the concentration of the chitosan increases with increase in time but due to the hydrophilic polymer i.e sodium alginate which help to detach the patch from mucosa. The correlation coefficients of all the three responses were found to be significant.

CONCLUSION: The objective of work was to formulate buccal patches of GRA.HCl using combination of hydrophobic and hydrophilic polymer such as chitosan and sodium alginate respectively. The mucoadhesive patch formulation itself is a critical process hence, it requires optimization at various stages. First stage was the simple formation of the chitosan film. This study reveals that the chitosan has good patch forming properties with varying amount.

A systematic study using 3^2 factorial designs was applied to optimize the formulation. The study revealed that the amount of chitosan and sodium alginate has significant effect on mucoadhesive properties such as swelling index, mucoadhesive strength, and mucoadhesion time and release characteristics of the drug.

In vitro cumulative % drug release of formulation F6 was found to be 95.81% upto 8 hr. The mucoadhesive strength was found to be 326.96N/M^2. *Ex vivo* release study showed 96.59% drug release. The dissolution study indicates release of the drug by following Higuchi model.

Swelling index was found to be 79.16%. The mucoadhesion strength was found to be 3.21 hr and % moisture absorption was found to be 167.35%. Response surface methodology study was carried out for mucoadhesion time, strength and *in vitro* drug release.

It was found that the composition of hydrophilic and hydrophobic polymer concentration plays a very important role in various buccal patch evaluation parameters because of their mucoadhesive and release controlling properties.

Thus, GRA.HCl buccal patches releasing drug upto 8 hr can be successfully formulated which can be comfortably used by the patients with improved bioavailability with sustained release characteristics. However there is need for further *in vivo* and stability studies.

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REFERENCES:

1. Das R, Ali KA, Bandopadhyay AK. Mucoadhesion and mucoadhesive tablets-a review. International Journal of Pharmaceutical Science Technology. 2011; 6(1): 64-115.
2. http://www.drugbank.ca/drugs/DB00889
3. British Pharmacopoeia. British Pharmacopoeia commission office. The department of health, Great Britain. London. 2009: 2846 - 2851.
4. Rowe RC, Sheskey PJ. Handbook of excipient. Sixth edition. Pharmaceutical press. 2009 :159 -161.
5. Punitha S, Girish Y. Polymers in mucoadhesive buccal drug delivery system – A review. International Journal of Research and Pharmaceutical Science. 2010; 1(2):170-186.
6. Morales JO, McConville JT. Manufacture and characterization of mucoadhesive buccal films. European Journal of Pharmaceutics and Biopharmapeutics. 2011;77:187–199.
7. Bazigha K. Rasool A. *In vitro* evaluation of miconazole mucoadhesive buccal films. International Journal of Applied Pharmaceutics. 2010; 2(4): 23-26.
8. Parmar HG, Jain JJ, Patel TK, Patel VM. Buccal patch: a technical note. International Journal of Pharmaceutical Science: Review and Research. 2010; 4(3):178-182
9. Mujoriya R, Dhahmade K. A Review on study of buccal drug delivery system. Innovative Systemic Disease and Engineering. 2(3):1-13.

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