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DEVELOPMENT AND OPTIMIZATION OF EFFERVESCENT TABLETS OF PROMETHAZINE

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ABSTRACT: The objective of present study was to develop effervescent tablets of promethazine (PMZ) for the treatment of emesis. Effervescent tablets were prepared by direct compression method and were optimized using 3^2 full factorial design. Amount to sodium starch glycolate(X1) and amount of sodium bicarbonate (X2) were selected as independent variables, whereas disintegration time (Y1), amount of carbon dioxide (Y2) and drug release in 5 minutes (Y3) were selected as dependent variables. All the batches were also evaluated for general post compression evaluation of tablet such as- weight variation, thickness, friability and hardness. From the results of design batches, best batch was selected and evaluated for in vivo pharmacokinetic study in a rabbit model. The disintegration time ranged from 58.67±0.27sec to 228.67± 0.67sec while amount of carbon dioxide ranged from 0.1±0.082 gm to 0.29±0.061gm in all the design batches. From the results of design batches, batch F9 was selected as optimized batch due to higher amount of carbon dioxide released and faster drug release as compared to other batches. Batch B4 was showing higher AUC and C_{max} while lower t_{max} as compared to drug suspension while performing *in vivo* study of optimized batch in a rabbit model. The study concluded that the combination of sodium starch glycolate and sodium bicarbonate approach for development of effervescent tablet aids to achieve faster disintegration and faster drug release property for PMZ.

INTRODUCTION: Promethazine (PMZ), (RS-dimethyl [1-methyl-2-(phenothiazone-10-yl) ethyl] amine hydrochloride), is a first-generation antihistamine drug, used in the treatment of motion sickness and emesis associated with a wide variety of chemotherapy and radiotherapy regimens.

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Oral bioavailability of PMZ from conventional tablet formulations is highly variable due to poor gastrointestinal absorption in motion sickness, impaired gastric emptying and extensive first pass metabolism. In emetic condition, loss of drug occurs which causes therapeutic failure, thus retention of an oral dose is essential for better absorption of drugs and their therapeutic actions [1-3]. Tablet formulations are having higher onset of action as compared to liquid formulations and also not appropriate formulation in case of emesis. While liquid dosage form is not preferable for drugs which are having poor stability in solution form or in water. Effervescent formulation can be a better alternative compared to conventional tablet

and liquid formulations. Stability, dose accuracy and portability can be achieved by the tablet formulation and palatability can be achieved by converting them in liquid dosage form before administration. Apart from this, it also exhibits advantages like a large dose of the API can be incorporated. Bitter taste can be modified by adding suitable sweeteners and flavors in formulation [4, 5].

Effervescence is described as expulsion of carbon dioxide gas from a fluid due to chemical reaction. This effect starts when formulation come in contact with water which works as catalyzing agent. Effervescent tablets need to be dissolved in water before administration. The tablet is promptly broken down by releasing carbon dioxide in water. Carbon dioxide produces by effervescent reaction increases the penetration of active substance into the paracellular pathway and consequently their absorption. The effervescent formulation does not come in direct contact with the gastrointestinal tract and thus such dosage forms are useful for this kind of patient. It decreases the onset of action, due to faster absorption of formulation in liquid dosage form, as compared to tablet formulations [4, 6].

Although, effervescence tablet formulations are having several advantages over conventional formulation, however, their production is associated with numerous problems. This is due to moisture sensitive ingredients used in the formulation for effervescence like- organic acid and alkali carbonate or bicarbonate salts. Thus, controlled environmental conditions like humidity and temperature is required while production of effervescent products. If this processing parameter cannot be controlled, premature reaction between acid and alkali can occur, which leads to stability issues.

Direct compression method is most beneficial for this dosage form as it gives less material contact with environment. Selection of material for direct compression methods depends on the flow properties of materials. The API has poor flow properties so it is required to select the excipients which improve flow ability. The combination of excipients can be used to increase the flow properties [7].

Thus, the aim of present study was to develop an effervescent tablet formulation of PMZ which shows a quick onset of action with less variable bioavailability in motion sickness and emesis conditions. It was presumed that the effervescent formulation might immediately release drug and improve the drug bioavailability. The effervescent formulation was systematically optimized using 3^2 full factorial design and optimized formulation was also evaluated *in vivo* using a rabbit model.

MATERIALS AND METHODS:

Materials:

Promethazine (PMZ) was procured as a gift sample from Cadila Pharmaceutical Ltd., Ahmedabad. Citric acid, tartaric acid, sodium bicarbonate, mannitol, sodium starch glycolate, polyethylene glycol 6000(PEG 6000) and sucrose were procured from Merck India Ltd., Mumbai, India. All the reagents used were of analytical grade.

Preparation of Effervescent Tablets:

PMZ, citric acid, tartaric acid, sodium bicarbonate, mannitol, sodium starch glycolate, poly ethylene glycol 6000 and sucrose were weighed and transferred in double cone mixture (Kalweka, Karnavati Engineering Ltd., India) for 15 min and then passed through sieve 40#. The powder was directly compressed to prepare tablets (punch diameter 8 mm) using a rotary tablet compression machine (RIMEK Mini Press II, Make: Karnavati Engineering, India). Developed tablets were evaluated for different parameters as per Pharmacopoeia.

Experiment Design:

To study the effect of factors, identified during preliminary trials, on the various properties of effervescent tablets, experiments were systematically conducted by employing 3^2 factorial designs. Design Expert® software (trial version 7.1.2, Stat-Ease, Inc., Minneapolis, MN) was used to graphically express the influence of each factor on the response by generating the response surface plots. The amount of sodium starch glycolate (X_1) and the amount of sodium bicarbonate (X_2) was selected as independent variables. The dependent response variables measured were disintegration time, amount of carbon dioxide and % drug release after 5 min. The composition of design batches and

levels of independent variables in coded as well as in actual form is shown in **Table 1** and **Table 2** respectively. The polynomial equation created by design is as follows:

$Yi=b_0+b_1X_1+ b_2X_2+ b_{12}X_1X_2+ b_1X_1^2+ b_2X_2^2$ .... (1)

where Y_i is the dependent variable; b_0 is the intercept; b_1, b_2, b_3, b_{12}, b_{23}, b_{13} are the regression coefficients; and X_1 and X_2 are the independent variables. All the batches were prepared and evaluated in triplicate (n=3)

TABLE 1: COMPOSITION OF PMZ EFFERVESCENT TABLETS

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
PMZ	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
Citric Acid	25	25	25	25	25	25	25	25	25
Tartaric Acid	25	25	25	25	25	25	25	25	25
Sodium Starch Glycolate	3	3	3	9	9	9	15	15	15
Sodium Bicarbonate	75	125	175	75	125	175	75	125	175
Sucrose	20	20	20	20	20	20	20	20	20
PEG 6000	9	9	9	9	9	9	9	9	9
Mannitol	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
Total	300	300	300	300	300	300	300	300	300

*All the quantities are in mg.

TABLE 2: VARIABLE AND THEIR LEVELS IN 3^2 FACTORIAL DESIGN

Independent variables	Levels		
	Low	Medium	High
X_1= amount of sodium starch glycolate (mg)	3	9	15
X_2= amount of sodium bicarbonate (mg)	75	125	175
Transformed values	-1	0	1
Dependent variables			
Y_1= Disintegration time			
Y_2= Amount of carbon dioxide			
Y_3= % Drug release after 5 min			

Selection of optimized formulation was done after considering the results of dependent variables of the experimental design batches. The batch with lower disintegration time and carbon dioxide and drug release in 5 minutes will be considered as optimized batch. The selected dependent variables are correlated with each other because the higher amount of released carbon dioxide results in faster bursting of tablets and hence lower disintegration time and faster drug release property.

Evaluation of tablets:

Flow Properties of Effervescent Powder:

Tap Density:

Powder blend of all formulations batches F1 to F9 were evaluated for tap density, angle of repose and carr's index. Tap density was performed in the tap density tester (Model: ETD-1020, Make: Electrolab). 10 gm of powder blend was taken in the cylinder and instrument was started. The 100 times tapping was done and the volume of the powder was measured. The tap density was calculated using equation (2) given below-

$$TapDensity = \frac{w}{v} \quad \text{..... (2)}$$

Where w = weight of powder blend and v = volume of powder blend

Angle of Repose:

5gm powder blend was weighed and filled in the glass funnel. The funnel was fit to stand at a fix height from base (3 cm). Powder passed from the funnel was collected on graph paper. When powder was passed from funnel, the height of the piles and diameter was measured. The angle of repose was calculated using the following equation (3)

$$Angleofrepose = tan\theta = \frac{h}{r} \text{..... (3)}$$

Where tan θ = angle of pile; h = height of pile and r = radius of pile.

Carr's index was calculated using given equation (4)

$$Carr's Index = 100\ [(\rho t - \rho b)/\rho t] \text{ ..... (4)}$$

Where ρ_t = tapped density and ρ_b = bulk density

Post Compression Evaluation of Tablet:
Weight variation study of the tablets was performed by accurately weighing the 10 tablets individually using digital weighing balance and calculating the average weight of the tablets. Individual weight of tablets was compared with the average weight of the tablets [8]. Hardness of the tablet was studied using hardness tester (DHT-250, Cambell Electronics Machine, Thermonik) by calculating the force required to split a tablet by compression in the diametric direction. Same instrument was used to measure diameter and thickness of the tablets. Friability was measured using Roche friabilator USP at 25 rpm for 4 min [9-11].

Disintegration Study:
The tablet disintegration time was measured as per pharmacopoeial procedure. The beaker of 250ml was filled with 200 ml of water and three tablets of developed formulations were added in this beaker. The time required for a tablet to disintegrate was determined using visual observation [9-11].

Amount of Carbon Dioxide:
The amount of carbon dioxide was measured by the method developed by G. Rajalakshmi et al. 10% sulfuric acid solution was prepared in distilled water. 100ml of prepared sulfuric acid solution was taken in a beaker of 250ml and weight of beaker was taken. One tablet was added in a beaker and tablet was observed for complete release of carbon dioxide from the tablet. Again weight of the beaker was determined and the difference in weight before and after release of carbon dioxide shows the amount of carbon dioxide generated [12, 13].

pH of the Solution:
200 ml purified water was taken in the glass beaker at room temperature. The effervescent tablet was kept in the beaker which allowed it completely to dissolve. The pH was measured using digital pH apparatus (Model: Mettler Toledo, Make: Japan).

***In-vitro* Dissolution Studies:**
The dissolution study was done in 500 ml of 0.01 M HCl buffer media at $37^oC \pm 2^oC$ using USP apparatus II (TDT08L, Dissolution Tester (USP), Electrolab) at 50 RPM. Samples were withdrawn at time intervals of 5, 15, 30, 45, 60, 90, and 120 min. The same amount of fresh dissolution medium was replaced after withdrawal of the sample. Drug content was analyzed at 249 nm by UV double beam spectrophotometer (UV 1800 Shimadzu Scientific Instrument, Japan). The cumulative percent of drug released was calculated using a calibration equation generated from the standard curve and plotted as percent cumulative drug released versus time [8].

***In -vivo* Study:**
The *in vivo* pharmacokinetics study was carried out on the rabbit animal model (Protocol No: RPCP/IAEC/2013-2014/R-28). *In vivo* pharmaco kinetic study was performed by dividing the animals in 2 groups (n=6). Animals were fasted over night and were placed in a restraining device (rabbit holder) before administration of reference (drug solution in water) and test (solution of optimized effervescent tablet) formulations. Formulations were administered using a feeding needle. Blood samples were collected from a marginal ear vein and collected with the help of a syringe attached to a hypodermic needle. For smooth blood collection, syringe was removed from the needle and cannula was closed to prevent blood clotting. The cannula was flushed with sodium citrate solution before closing to prevent blood clotting. 1ml of blood was withdrawn at time intervals of 30, 60, 90, 120,150 and 180 min through the cannula into 2 ml micro centrifuge tubes which contain 0.5 ml of sodium citrate solution [14].

Estimation of PMZ in Blood Sample:
Plasma aliquots of 0.5 ml was taken from rabbit plasma for analysis of PMZ and transferred into a 2-mL centrifuge tube. In the same centrifuge tube, 1ml of methanol was added and vortexed using a cyclomixer (Model: CM101, Make: Remi Laboratory Ltd, India) for 15 min. After vortex, the tube was centrifuged at 10,000 RPM for 10 min. The supernatant was taken in the cuvette for estimation of drug content. PMZ was estimated at 249 nm excitation wavelength using a fluorescence spectrometer (Model: LS 55 Make: Perkin Elmer)

RESULTS AND DISCUSSION:
Flow Properties of Powder: Characteristics of powder blend was evaluated for tap density, angle

of repose and carr's index. The tap density of all formulation was found between 0.62±0.02 to 0.8±0.05 gm/ml (**Table 3**). The carr's index was in range from 08.9±0.29 to 26.5±0.15 % (Table 3) and as per pharmacopoeia carr's index is passable when it is ±25%. The angle of repose of all formulation was from 30.96±0.19 to 44.71±0.9 **(Table 3)** and pharmacopoeial requirement for passable is ±45. The batch F9 showed carrs's index 15.38±0.55% which is in the category of good compressibility of powder. The angle of repose of batch F9 was 31.38±0.25 that is also in the range of good flow ability of powder. The overall powder of all formulations was exhibit good flow as per the pharmacopoeia [8].

Post Compression Evaluation of Tablet:

The results of weight variation study, shown in **Table 3**, were not showing a significant difference in the weight of individual tablet from the average value. The diameter was found in the range of 7.07±0.129mm to 8.28±0.159mm and the thickness was between 3.45±0.037mm to 4.18±0.091mm. The hardness and friability were shown in **Table 3** for all the formulation. Hardness was found in a range of 2.68±0.209kg/cm^2 to 5.52±0.12kg/cm^2 whereas friability was found in a range of 0.36±0.012% to 0.68±0.09% which is (that is less than 1%) in the acceptable limits.

Data Analysis:

Results of experimental design batches (F1 to F9) were shown in **Table 4**. 3^2 factorial experimental design was used to optimize the amount of sodium bicarbonate and sodium starch glycolate to get the faster disintegration time and a higher amount of carbon dioxide and drug release after 5 min. The results of statistical analysis for design batches were obtained by Design Expert® software and were shown in **Table 4**. The polynomial equation generated for each response by software was described in equation 5-7 and response surface plot for each response was shown in **Fig. 1-3.**

TABLE 3: CHARACTERISTIC OF POWDER BLEND AND EFFERVESCENT TABLET

Batch Code	Friability %	pH	Tapped Density (gm/ml)	Angle of Repose (θ)	Carr's Index (%)	Weight Variation (g)	Hardness (kg/cm2)	Thickness (mm)	Diameter (mm)
F1	0.68±0.09	6.75±0.04	0.67±0.06	44.71±0.90	20.09±0.19	298.00±1.41	5.52±0.12	3.99±0.04	7.96±0.59
F2	0.64±013	7.01±0.09	0.73±0.07	43.83±0.56	16.15±0.86	298.18±1.29	5.03±0.106	3.73±0.019	7.96±0.046
F3	0.56±0.009	7.28±0.17	0.8±0.03	30.96±0.19	8.9±0.29	297.27±1.93	2.68±0.209	3.45±0.037	7.07±0.129
F4	0.47±0.014	6.1±0.18	0.8±0.06	35.75±0.29	17.21±0.69	297.27±1.93	4.52±0.129	3.49±0.108	8.03±0.239
F5	0.36±0.012	6.42±0.09	0.73±0.02	36.13±0.14	16.13±0.44	298.18±1.29	3.94±0.059	3.69±0.082	8.04±0.024
F6	0.65±0.022	6.71±0.16	0.8±0.05	36.5±0.45	26.5±0.15	299.09±.64	2.23±0.096	3.53±0.106	8.09±0.095
F7	0.48±0.016	6.3±0.12	0.62±0.10	32.21±0.08	12.21±0.18	296.36±2.57	2.08±0.027	4.15±0.042	8.20±0.048
F8	0.47±0.086	6.45±0.09	0.67±0.04	26.56±0.04	14.56±0.14	301.82±1.29	3.26±0.048	4.18±0.091	8.26±0.024
F9	0.55±0.018	6.5±0.14	0.62±0.02	31.38±0.25	15.38±0.55	296.36±2.57	4.69±0.064	3.99±0.014	8.28±0.159

TABLE 4: 3^2 FACTORIAL DESIGN MEASURED RESPONSES

Batch Code	X_1	X_2	Disintegration time (sec)	Amount of Carbon Dioxide (g)	Drug release after 5 min (%)
F1	3	75	228.67± 0.67	0.1±0.07	89.71±0.23
F2	3	125	191.67±0.37	0.18±0.03	92.15±0.37
F3	3	175	176±0.656	0.26±0.06	93.55±0.49
F4	9	75	129.33±0.87	0.11±0.07	85.85±0.74
F5	9	125	117±0.13	0.17±0.01	91.11±0.82
F6	9	175	72.33±0.57	0.29±0.06	88.55±0.34
F7	15	75	75.67±0.97	0.1±0.08	93.55±0.56
F8	15	125	58.67±0.27	0.12±0.04	93.98±0.90
F9	15	175	61.67±0.47	0.25±0.03	96.55±0.43

TABLE 5: RESULTS OF P VALUE AND REGRESSION COEFFICIENT

Responses	p values of coefficients						
	b_0	b_1	b_2	b_{12}	b_1^2	b_2^2	R^2
Disintegration time	0.0131	0.0021	0.2438	0.6045	0.1091	0.0697	0.9750
Amount of carbon dioxide	0.0055	0.1409	0.0026	0.1803	0.1227	0.0018	0.9861
Drug release in 5 min	0.0567	0.0854	0.1548	0.9655	0.8474	0.0114	0.9319

Effect of Disintegration Time:

The disintegration time ranged from 58.67±0.27sec to 228.67± 0.67sec for all the formulations.

Disintegration time (Y_1) = +127.33-66.72*X_1-9.56*X_2+4.67*X_1X_2+25.84X_1^2-31.67X_2^2 ..... (5)

The polynomial equation depicts that the magnitude of coefficient of X_1 and X_2 shows the negative effect which means that as the amount of both the parameters increased, disintegration time was decreased. This might be due to faster disintegration tablet because of the higher amount of these ingredients. X_2 had shown a non-significant effect (p>0.05, **Table 5**) where as X_1 had shown a significant effect on the (p<0.05, **Table 5**) disintegration time. The overall model was significant because the p value was <0.05. Similar results could be observed in the 3D surface plots (**Fig. 1**).

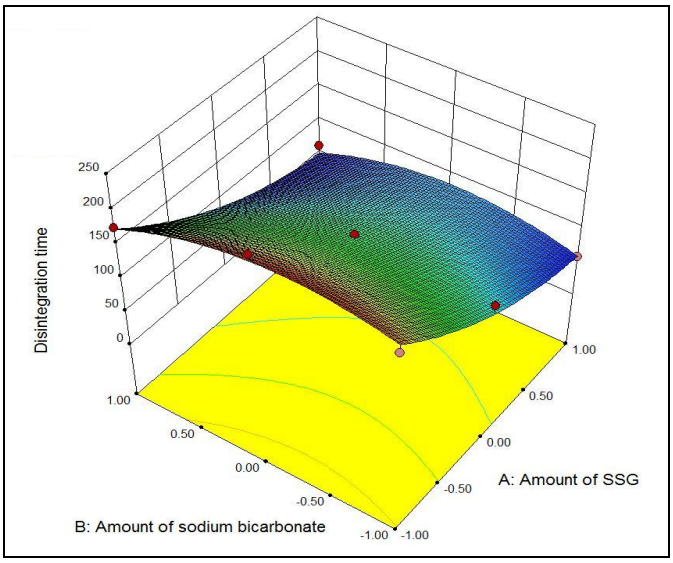

FIG. 1: 3D SURFACE PLOT FOR DISINTEGRATION TIME

Amount of Carbon Dioxide:

The amount of carbon dioxide ranged from 0.1±0.07 gm to 0.29±0.06 gm for all the formulations F1 to F9.

Amount of CO_2(Y_2) = +0.12-0.012* X_1+0.055* X_2+0.012*X_1X_2-0.022X_1^2+0.11X_2^2 .....(6)

The polynomial equation depicts that the magnitude of coefficient of X_2 show positive effect and X_2 had a significant effect (p<0.05, **Table 5**) on the amount of carbon dioxide. The overall model was significant because the p value was <0.05. The values of interactive term for X_1 and X_2 were positive. From the 3D surface plot, as shown in **Fig. 2**, it can also be concluded that the amount of carbon dioxide increases with increase in the amount of sodium bicarbonate. Similar type of results were obtained by Amela et al and Yanze et al while developing the effervescent formulation containing citric acid and sodium bicarbonate [12, 15].

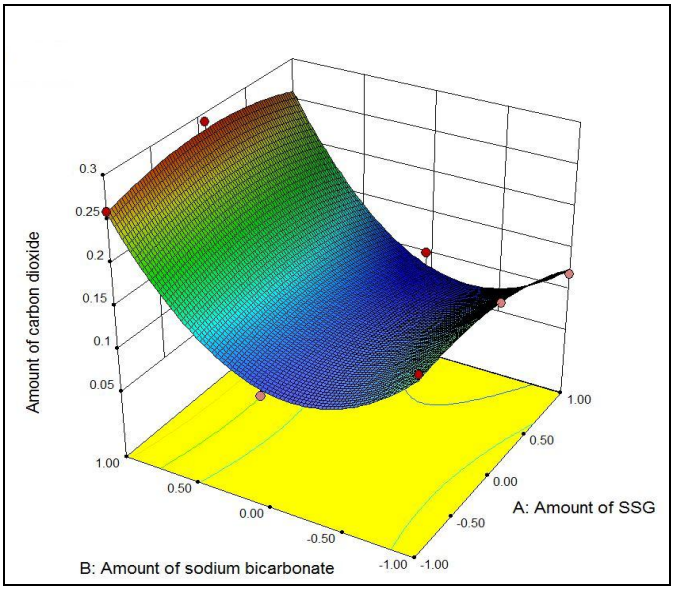

FIG. 2: 3D SURFACE PLOT FOR AMOUNT OF CARBON DIOXIDE

Drug Release After 5 Min:

Drug release after 5 min was obtained from85.85±0.74% to 96.55±0.43% for all the formulations F1 to F9.

Drug release after 5 min. (Y_3) = +88.17+1.43* X_1+1.07* X_2+0.033* X_1 X_2-0.20X_1^2+5.45X_2^2.... (7)

The polynomial equation depicts that the magnitude of coefficient of X_1, and X_2 shows a positive effect on drug release after 5 min. From all 3D surface plots (**Fig. 3**) suggested that the higher amount of SSG and sodium bicarbonate found faster drug release. All the batches were showing more than 85% drug releases after 5 min. Drug release profile of the design batches is shown in **Fig.4**.

Tekade et al, made the effervescent tablet of diclofenac sodium using the sodium carbonate and sodium bicarbonate with citric acid was showing drug release. Use of two acid sources might be the reason for faster drug release [15].

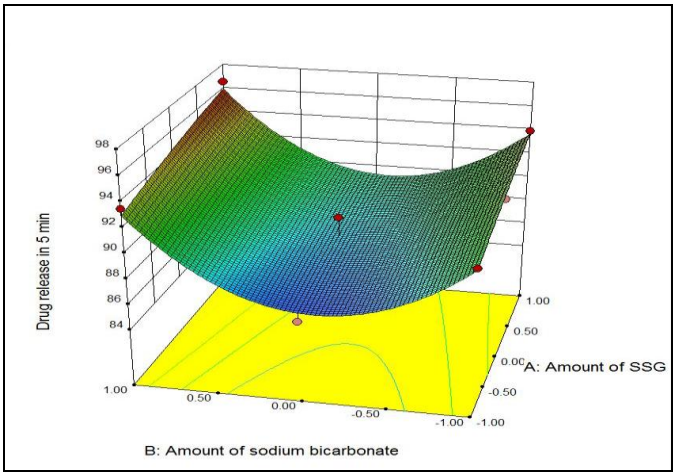

FIG. 3: 3D SURFACE PLOT FOR DRUG RELEASE AFTER 5 MIN

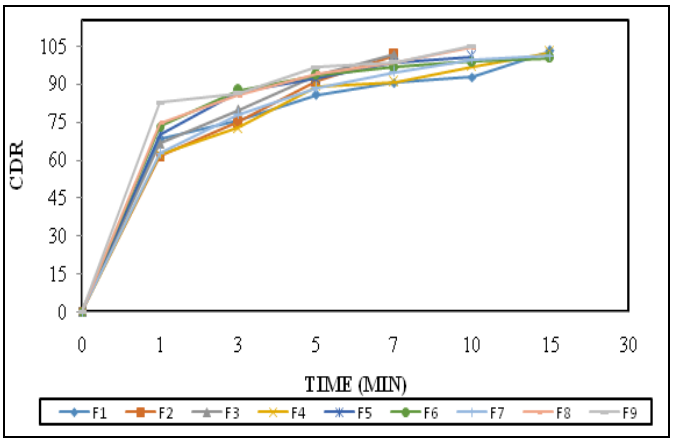

FIG.4: COMPARATIVE DRUG RELEASE OF ALL FORMULATIONS

From the results of design batches, batch F9 was selected as optimized batch due to higher amount of carbon dioxide release and faster drug release as compared to other batches. Disintegration time, amount of release carbon dioxide and drug release in 5 minutes for batch F9 were found 61.67±0.47sec, 0.25±0.03 and 96.55±0.43% respectively.

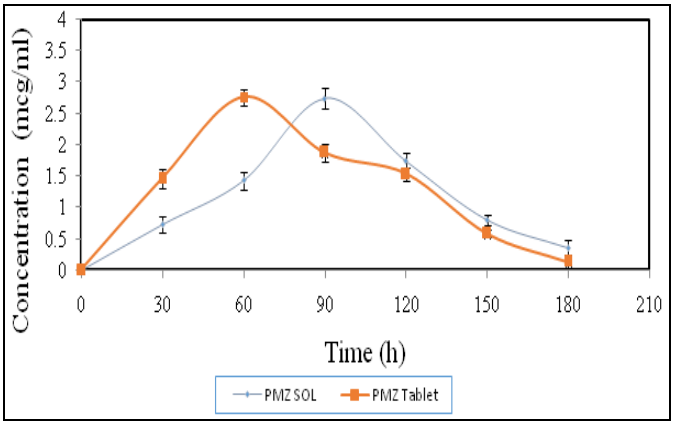

FIG. 5: DRUG RELEASE IN RABBIT PLASMA.

***In -vivo* Study:**

The results of *in vivo* study using fluorescence spectrometer was shown a good correlation and linear relationships, in plasma concentration ranging from 500ng/ml to 5500 ng/ml. The method used for analysis was reproducible with high precision which could be concluded from its percentage accuracy for intra-day and inter-day studied batches and were complied within the limit of 85-115%.

After administration of both reference and test formulations to the rabbits, blood samples were collected from the rabbits at a definite time interval. The maximum plasma concentration (C_{max}), time to reach the maximum plasma concentration (t_{max}), area under the drug plasma concentration-time curve up to 2h post-administration (AUC 0-2 h) and the elimination half-life ($t_{1/2}$) was calculating using non compartmental analysis. These data are shown in **Table 6**. From the **Fig. 5**, t_{max} found higher in case of effervescent tablet solution of batch F9 compared to the drug solution. This might be due to generation of carbon dioxide produces by effervescent reaction which increases the penetration of active substance into the paracellular pathway and consequently their absorption. Eichman JD and Robinson JR studied effect of effervescence on permeability of various hydrophobic and hydrophilic drugs. They concluded that carbon dioxide reduces the transepithelial electrical resistance (TEER) which causes the epithelium disruption and lead to change in paracellularpathway [16].

TABLE 6: PHARMACOKINETICS PARAMETERS OF REFERENCE AND OPTIMIZED BATCH FORMULATIONS

Parameter	Reference	Optimized batch (F9)
AUC (0-180 min)	197.25	236.56
t max (Min)	90	60
C max (mcg/ml)	2.74	2.76

CONCLUSION: The study concluded that the combination of sodium bicarbonate and sodium starch glucolate approach for development of effervescent tablet aids to achieve faster disintegration as well as drug release property for PMZ. The 3^2 Full Factorial design was employed for the optimization and study the effect of process

parameters and their interaction on the effervescent formulation were studied. Optimized batch showed faster disintegration and drug release as compared to other batches. Moreover higher AUC and C_{max} while lower t_{max} was observed as compared to drug suspension while performing *in vivo* study of optimized batch in a rabbit model. Thus, it could be concluded that combination of SSG and sodium bicarbonate helps to develop effervescent tablets. Use of experimental design might be helpful to develop an effervescent formulation with desired characteristics like faster disintegration and drug release with minimum efforts in the shortest time.

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REFERENCES:

1. Sharma S, Sharma N and Gupta GD: Formulation of fast-dissolving tablets of promethazine theoclate. Tropical Journal of Pharmaceutical Research 2010; 9: 489-97.
2. McDonough J, Persyn J, Nino J, Dixon H, Boland E, Wang Z and Putcha L: Microcapsule-gel formulation of promethazine HCl for controlled nasal delivery: A motion sickness medication. Journal of Microencapsulation 2007; 24: 109-16.
3. Kavitha K, Sandeep D, Yadawad M and Mangesh M: Formulation and evaluation of oral fast dissolving tablets of promethazine HCL by sublimation method. International Journal of PharmTech Research 2011; 3: 660-3.
4. Aslani A and Jahangiri H: Formulation, characterization and physicochemical evaluation of ranitidine effervescent tablets. Advanced Pharmaceutical Bulletin 2013; 3: 315-22.
5. Stahl H. Effervescent dosage manufacturing. Pharmaceutical Technology Europe 2003: 25-28.
6. Bodmeier RA, Swarbrick J and Boylan J: Encyclopedia of pharmaceutical technology. 3 ed: Informa Healthcare 2006. p. 1454-65.
7. Rotthäuser B, Kraus G and Schmidt PC: Optimization of an effervescent tablet formulation containing spray dried L-leucine and polyethylene glycol 6000 as lubricants using a central composite design. European Journal of Pharmaceutics and Biopharmaceutics: Official Journal of Arbeitsgemeinschaft fur Pharmazeutische Verfahrenstechnik eV 1998; 46: 85-94.
8. Indian Pharmacopoeia- 2014: Indian Pharmacopoeia Commission, Ministry of health and family welfare, Government of India, Ghaziabad, India. p. 43.
9. Jacob S, Shirwaikar A and Nair A: Preparation and evaluation of fast-disintegrating effervescent tablets of glibenclamide. Drug Development and Industrial Pharmacy 2009; 35: 321-28.
10. Nagendrakumar D, Raju S, Shirsand S, Para M and Rampure M: Fast dissolving tablets of fexofenadine HCl by effervescent method. Indian Journal of Pharmaceutical Sciences 2009; 71: 116-19.
11. Swamy P, Divate S, Shirsand S and Rajendra P: Preparation and evaluation of orodispersible tablets of pheniramine maleate by effervescent method. Indian Journal of Pharmaceutical Sciences 2009; 71: 151-54.
12. Amela J, Salazar R and Cemeli J: Methods for the determination of the carbon dioxide evolved from effervescent systems. Drug Development and Industrial Pharmacy 1993; 19: 1019-36.
13. Rajalakshmi G, Vamsi C, Balachandar R and Damodharan N: Formulation and evaluation of diclofenac potassium effervescent tablets. International Journal of Pharmaceutical and Biomedical Research 2011; 2: 237-43.
14. Gauniya A, Das S, Mallick S and Basu S: Comparative bioavailability studies of citric acid and malonic acid based aspirin effervescent tablets. Journal of Pharmacy and Bioallied Sciences 2010; 2: 118-20.
15. Tekade BW, Jadhao UT, Thakare VM and Bhortake LR: Formulation and evaluation of diclofenac sodium effervescent tablet. Innovations in Pharmaceuticals and Pharmacotherapy 2014; 2: 350-58.
16. Eichman JD and Robinson JR: Mechanistic studies on effervescent-induced permeability enhancement. Pharmaceutical Research. 1998; 15: 925-30.

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