IJPSR (2013), Vol. 4, Issue 6 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 22 February, 2013; received in revised form, 07 April, 2013; accepted, 28 May, 2013

FORMULATION AND EVALUATION OF ANTACID ANALGESIC TABLET

N.D. Banerjee*, S .S. Shukla and S.R. Singh

Dr. L.H. Hiranandani College of Pharmacy, CHM Campus, Ulhasnagar- 03, Maharashtra, India

Keywords:

Paracetamol, Hyperacidity, Palatability, Dissolution, Effervescence, Factorial design

Correspondence to Author:

N.D. Banerjee

Research Scholar, Dr. L.H. Hiranandani College of Pharmacy, CHM Campus, Ulhasnagar- 03, Maharashtra, India

E-mail: banerjeenandini89@gmail.com

ABSTRACT: The present study deals with formulation of a combined analgesic and antacid effervescent tablets. Paracetamol is the model drug used. It is poorly soluble in the water and hence the formulation is in the form of an effervescent tablet so that the disintegration time of the drug is not hindering the action. The mixture of magnesium and aluminium hydroxide is used as the model antacid. The present research work describes a combination dosage of the antacid and analgesic which is useful in case of hyperacidity related severe headaches. In the formulation citric acid and tartaric acid along with sodium bicarbonate is being used as the effervescent mixture. It not only aids in solving the disintegration problem but also increases the palatability due to its acidulous taste. It severs advantages of the tablet dosage form and has the bioavailability of that of the liquid formulation. The combination can also be dispensed in the form of granules in unit sachets. The release character was studied using the disintegration and the dissolution studies conducted. The amount of the active available from the dosage after the release was studied using the UV spectrophotometer and also the values of individual assays conducted. The formulation was seen to have good release and availability of both the active moieties.

INTRODUCTION: The oral dosage forms are the most popular way of taking medication despite having some disadvantages like slow absorption and thus onset of action is prolonged. This can be overcome by administrating the drug in liquid from but, many APIs have limited level of stability in liquid form.

So, effervescent tablets acts as an alternative dosage form. The tablet is added into a glass of water just before administration and the drug solution or dispersion is to be drunk immediately.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.4(6).2327-35

Article can be accessed online on: www.ijpsr.com

The tablet is quickly broken apart by internal liberation of CO_2 in water due to interaction between tartaric acid and citric acid with alkali metal carbonates or bicarbonates in presence of water. Due to liberation in CO_2 gas, the dissolution of API in water as well as taste masking effect is enhanced. The advantages of effervescent tablets compared with other oral dosage forms includes an opportunity for formulator to improve taste, a more gentle action on patient's stomach and marketing aspects. These tablets can be produce by wet or heat fusion.

The manufacturing shall be done under controlled climatic condition to avoid effervescent reaction. The packaging is done under 25% RH at 25ºC. Different carbonates, acids and buffers were used to attain good effervescence in short time and to obtain a clear solution and to give maximum therapeutic effect in short span of time when taken orally [1, 2].

Advantages of Effervescent Tablets: Effervescent tablets are outstanding because [3];

(a) They offer an attractive administration and also improve the absorption of the active drug by previous dissolution in a buffered medium,

(b) Effervescent system can buffer the aqueous solution of drug, so that the stomach pH increases (becomes less acidic) and thus prevent the degradation or inactivation of the active ingredient. This buffering effect (via carbonation) induces the stomach to empty quickly–usually within 20 minutes into small intestine and results in maximum absorption of active ingredient,

(c) Effervescent tablets have major advantage that the drug product is already in solution at the time it is consumed. Thus, the absorption is faster and more complete than with conventional tablet,

(d) They dissolve fully in a buffered solution. Reduced localized contact in upper GIT leads to less irritation and greater tolerability. Buffering also prevents gastric acids from interacting with drugs themselves, which can be a major cause of stomach and oesophageal upsets,

(e) They retain their palatability after lengthy storage, essentially flavourings so they taste much better than a noneffervescent in water. Moreover, they produce fizzy tablets, which may have better consumer appeal than the traditional dosage forms,

(f) Excellent stability is inherent with effervescent formulations, particularly surpassing liquid forms,

(g) Drugs delivered using effervescent technology have predictable and reproducible pharmacokinetic profiles that are more consistent than tablets or capsules,

(h) Effervescent components aid in improving the therapeutic profiles of active ingredients. They also help in solubilization of poorly soluble drugs,

(i) Effervescence induces penetration enhancement of broad range of compounds ranging in size structure and other physiological properties. Effervescent blend can be used to obtain programmed drug delivery i.e. floating tablets.

(j) In remote areas, especially where parenteral forms are not available due to prohibitive cost, lack of qualified medical staff, effervescent tablets could become an alternative e.g., the use of chloroquine phosphate effervescent tablets for epidemic diseases like malaria and viral fever,

(k) To solve the problems of physicochemical stability and high cost of transporting syrups, effervescent tablets provide a realistic solution.

Objective: The urgent need for this today is to give instant relief from hyperacidity which is usually accompanied by terrible head-ache. Headache due to acidity is caused mainly because of absorbing toxic products from the colon. At the time of constipation the un-eliminated and undigested food gets putrefied and it releases toxic materials, acids, etc. This toxins and gases get released into the blood and causes irritation in nerves and nerve cells mainly of head. This irritation of nerve cells in turn leads to headache.

In such cases, the physician's usually prescribes an antacid separately along with an analgesic. This can be avoided by just taking a single effervescent tablet containing both the actives. It also proves to be beneficial for geriatrics that has swallowing problem. As compared to the syrups for similar actions effervescent tablets would be more stable and less bulky. Also there would be less/ no chance of microbial growth along with dose accuracy [4].

In the study, Paracetamol is used in combination with Aluminium Hydroxide and Magnesium Hydroxide. Paracetamol will act as a quick acting analgesic. Aluminium hydroxide and magnesium hydroxide will act as efficient antacids. Granules ready for compression of individual constituents are prepared and compressed together to get an intact tablet which on addition to required quantity of water would disperse instantly.

MATERIALS AND METHODS:

Materials: Paracetamol, Aluminium Hydroxide, Magnesium Hydroxide, Citric Acid, Tartaric Acid, Sodium Hydroxide, and all the other chemical reagents used were of pharmaceutical grade.

Preformulation [5]: The overall Objective of Preformulation testing is to generate information useful to generate information useful to the formulation in developing desired, stable and bio-available dosage form.

1. **Melting Point Determination**: The melting point of paracetamol was determined for product identification [6].

2. **Drug- Excipient IR compatibility study**: The pure drug and its formulation along with excipient were subjected to IR studies. In the present study, potassium bromide pellet was employed using Shimadzu FTIR Spectrometer.

3. **Standard calibration curve**: The spectrum of paracetamol was determined using Shimadzu UV-1800 instrument [7].

Then the concentration curve of the same was obtained within a range of 2ppm to 12ppm. Accurately 10mg of paracetamol was dissolved with 2ml ethanol and then made up to 10ml with distilled water. Then 1ml was pipette out and diluted to 10ml to prepare a stoke solution of 100ppm. From the stoke solution further solutions of 2, 4, 6, 8, 10, 12 ppm was prepared and the absorbance was measured at 243.4 nm.

Method: The tablets were prepared by simple wet granulation technique [8].

All the ingredients were weighed and passed via sieve no. 20 to get free flowing powder (**Table 1**). The powders were geometrically mixed and then dough prepared with 10% PVA in IPA solution and passed through sieve.no.8 and dried for not more than 5mins. Then the granules were passed via sieve.no.14 and retained on sieve.no.20. The granules along with the post granulating substances are ready for compression. The tablets were compressed with 12 mm diameter flat face punch. The tablets were packed in stacked arrangement.

TABLE 1: COMPOSITION OF EFFERVESCENT TABLETS

INGREDIENTS	F1	F2	F3	F4	F5	F6
Paracetamol	350	350	350	350	350	350
Aluminium hydroxide	200	200	200	200	200	200
Magnesium hydroxide	200	200	200	200	200	200
Povidone	16.75	16.75	16.5	18.75	18.75	18.75
Citric acid	40.59	65.98	49.108	42.59	67.98	51.108
Tartaric acid	61.88	99.98	74.56	63.88	101.98	76.56
Sodium bicarbonate	121.51	195.16	146.2	123.51	197.16	148.2
PVA in IPA (10%)	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

All the weights are mentioned in mg.

Factorial design: Traditionally, pharmaceutical formulations are developed by changing one variable at a time. The method is time consuming and it is difficult to evolve an ideal formulation using this classical technique. Since the combination effects of independent variables are not considered. It is thus important to understand the complexity of pharmaceutical formulation by using established statistical tools such as factorial design.

Based on preliminary trails a 2^2 full factorial design was adopted to optimize the variables. In this design two factors were evaluated, each at two different levels, and experimental trials were performed at four possible formulations. The amount of povidone (X_1) and the amount of effervescent mixture (X_2) i.e. citric acid ,tartaric acid and sodium bicarbonate; were selected as independent variables and in vitro disintegration/ dispersion time as the response/ dependent variable. (**Figure 10, 11**)

Evaluation of Granules: (**Table 5**)

1. **Bulk density:** It is defined as mass of powder divided by the bulk volume. It depends on particle size distribution, particle shape, and tendency of particle to adhere to each other. A quantity of weighed granules was introduced in a 25ml measuring cylinder and the initial volume was noted. The Loose bulk density (LBD) was calculated using:

LBD= Weight of Granules / Volume of Packing

2. **Tap density:** After measuring the bulk density the same measuring cylinder was set into tap density apparatus. It was set at 300 taps drop per minute and operated for 500 taps. Volume was noted as Va and again tapped for 750 taps. This volume was noted as Vb.

The tap density is calculated by;

Tap Density= Weight of Granules / Tapped Volume

3. **Angle of Repose:** The frictional force in a loose powder or granules can be measured by angle of repose. It is defined as angle possible between the surface of a pile of the powder and the horizontal plane (**Table 2**) [12].

$\tan\theta = h/r$

Where θ = angle of repose, h= height of pile, r= radius of the base of pile

TABLE 2: RELATION BETWEEN ANGLE OF REPOSE AND THE FLOW PROPERTY

Angle of Repose (θ) (in degrees)	Flow Property
Less than 25	Excellent
25-30	Good
30-40	Passable
More than 40	Poor

A funnel was filled to the brim and the test sample was allowed to flow smoothly through the orifice under gravity. From the cone formed on the graph sheet the height and the radius of the pile was determined for the calculation of the angle of repose by the above mentioned formula.

4. **Compressibility index:** The % compressibility is determined by Carr's compressibility index (**Table 3**) [12].

TABLE 3: GRADING OF GRANULES FOR THEIR FLOW PROPERTIES ACCORDING TO CARR'S INDEX

Carr's index (%)	Flow
5-15	Excellent
12-16	Good
18-21	Fair to passable
23-25	Poor
33-38	Very poor
>40	Very poor

The % Carr's index is calculated using the following formula;

%Carr's Index= TD – BD / TD X 100

5. **Hausner's ratio:** It is also known as the Packing factor and is the ratio of tap density upon bulk density.

Evaluation Parameters of Tablets: (**Table 6**)

1. **Tablet Dimensions:** Thickness and diameter were measured using a calibrated dial calliper. Ten tablets of each formulation were evaluated.

2. **Hardness:** Monsanto hardness tester was used to evaluate hardness of tablet. The tester consists of a barrel containing a compressible spring held between two plungers. The lower plunger was placed in contact with the tablet, and a zero reading was taken. The upper plunger was then forced against a spring by turning a threaded bold until the tablet fractures. As the spring compressed, a pointer rides along a gauge in the barrel to indicate the force. The force of fracture was recorded, and the zero force reading was deducted from it. Ten tablets of each formulation were evaluated.

3. **Friability:** Roche friabilator was used to determine friability of the tablets. Twenty preweighed tablets were placed in the friabilator, which was then operated for 100 revolutions. The tablets were then dedusted and reweighed. The friability was computed by following formula:

F= (1 - Wo / W) X 100

Where, f = percentage friability, Wo = initial weight of 20 tablets, W = weight after friability testing

4. **Weight Variation:** Twenty tablets were selected randomly. Tablets were weighed individually and average weight was calculated. Then deviation of each tablet from average weight was calculated and percent deviation was computed.

5. **Disintegration Time:** It was performed in disintegration apparatus at 37.5^{0}C temperature and time was noted. Place one tablet into each tube and suspend the assembly in to the 1000 mL beaker containing water maintained at 37±2°C. The disintegration time is noted and is compared with IP specification [12] (**Figure 8**).

6. **Content Uniformity:** In this test, 20 tablets were randomly selected contained for sample, and the content uniformity was studied as per IP specification [12].

7. ***In vitro* Drug Release:** The dissolution test was carried out in distilled water. Aliquots were withdrawn at predetermined time intervals and after suitable dilutions absorbance were measured with the help of UV spectrophotometer at 243.3nm and the percentage drug released at various time intervals were calculated. Cumulative percentage drug release was calculated using an equation obtained from a standard curve (**Table 7, Figure 7**).

Also, the different drug release profiles were compared to get the release mechanism of the formulation (**Figure 9**).

RESULTS AND DISCUSSION:

Preformulation:

1. **Melting point:** The melting point of paracetamol was determined to be 170^{0}C.

2. **Drug- Excipient IR compatibility study:** (**Figure 1, 2, 3, 4**)

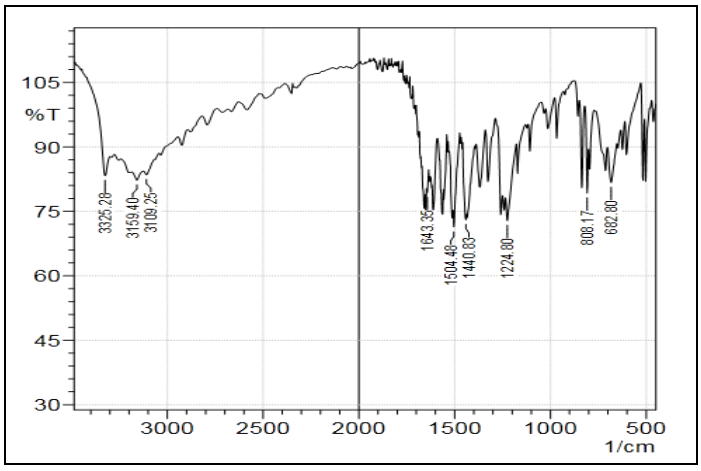


FIG. 1: IR CURVE OF PARACETAMOL

No.	Peak	Intensity	Corr. Int	Base (H)	Base (L)	Area	Corr. Are
1	682.8	81.68	8.572	702.09	653.87	3.226	1.099
2	808.17	79.23	13.917	821.68	800.46	1.003	0.47
3	1224.8	72.809	7.462	1234.44	1176.58	5.216	0.901
4	1440.83	73.019	4.47	1458.18	1436.97	2.336	0.546
5	1504.48	71.249	6.052	1508.33	1473.62	3.009	0.345
6	1643.35	79.332	2.46	1647.21	1635.64	1.047	0.08
7	3109.25	83.503	1.631	3124.68	3066.82	4.079	0.22
8	3159.4	82.246	2	3186.4	3132.4	4.27	0.249
9	3325.28	83.278	8.538	3421.72	3298.28	2.659	0.788

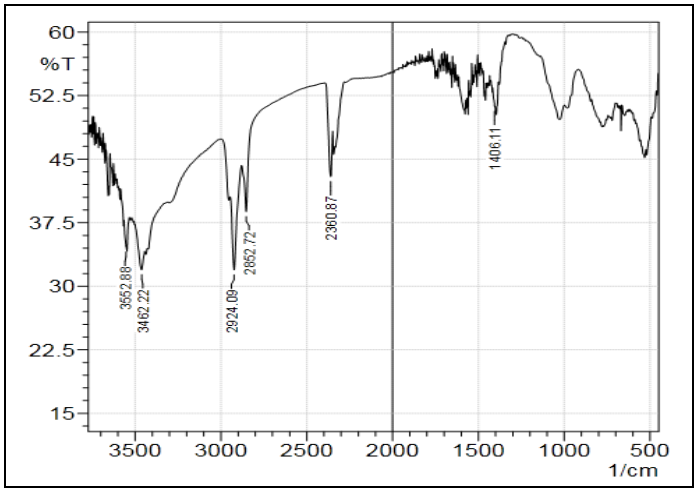


FIG. 2: IR CURVE OF ALUMINIUM HYDROXIDE

No.	Peak	Intensity	Corr. Int	Base (H)	Base (L)	Area	Corr. Are
1	1406.11	51.232	0.351	1417.68	1404.18	3.82	0.025
2	2360.87	42.921	6.862	2393.66	2349.3	14.171	1.224
3	2852.72	38.793	6.497	2879.72	2679.13	62.759	-1.347
4	2924.09	31.904	9.926	2947.23	2879.72	28.312	3.137
5	3462.22	31.935	3.188	3500.8	3444.87	26.218	1.192
6	3552.88	34.608	0.505	3564.45	3550.95	6.042	0.084

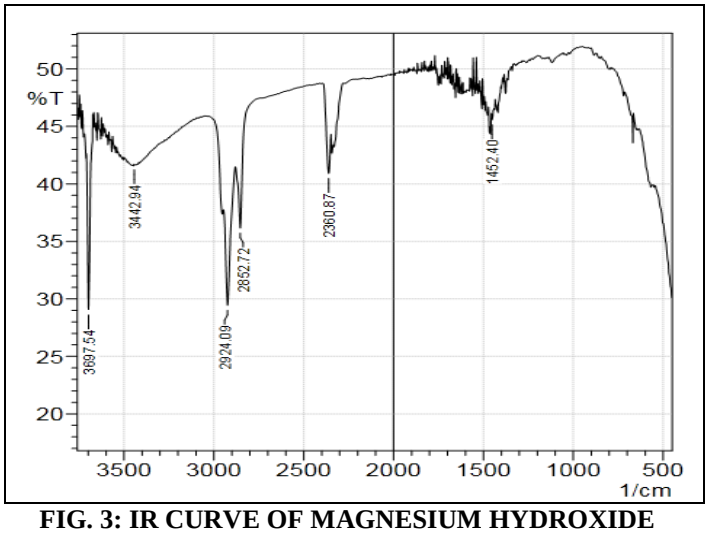


FIG. 3: IR CURVE OF MAGNESIUM HYDROXIDE

No.	Peak	Intensity	Corr. Int	Base (H)	Base (L)	Area	Corr. Are
1	1452.4	45.567	0.685	1456.26	1440.83	5.191	0.04
2	2360.87	40.91	4.473	2397.52	2349.3	16.886	0.842
3	2852.72	36.155	6.5	2879.72	2740.85	48.946	-0.046
4	2924.09	29.436	9.605	2947.23	2879.72	30.401	3.229
5	3442.94	41.658	0.038	3444.87	3441.01	1.466	0.001
6	3697.54	29.033	14.897	3711.04	3674.39	15.54	2.597

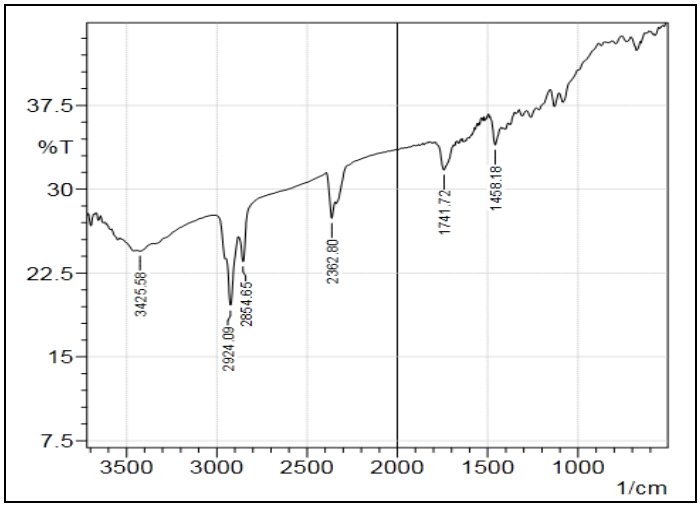


FIG. 4: IR CURVE OF FORMULATION (Paracetamol, Aluminium Hydroxide, Magnesium Hydroxide, Sodium Bicarbonate, Citric Acid, Tartaric Acid, Binder and Talc.)

No.	Peak	Intensity	Corr. Int	Base (H)	Base (L)	Area	Corr. Are
1	1458.18	33.943	1.362	1489.05	1444.68	20.201	0.321
2	1741.72	31.712	0.819	1789.94	1730.15	28.838	0.169
3	2362.8	27.384	2.43	2393.66	2345.44	25.884	0.777
4	2854.65	23.505	2.547	2879.72	2393.66	257.884	-7.238
5	2924.09	19.554	4.951	2949.16	2879.72	44.781	2.681
6	3425.58	24.466	0.185	3444.87	3348.42	58.453	0.112

3. Preparation of Standard Calibration Curve:

UV spectrum: The drug content and release of paracetamol from the formulation was determined by using UV Spectrophotometer (**Figure 5, 6, Table 4**).

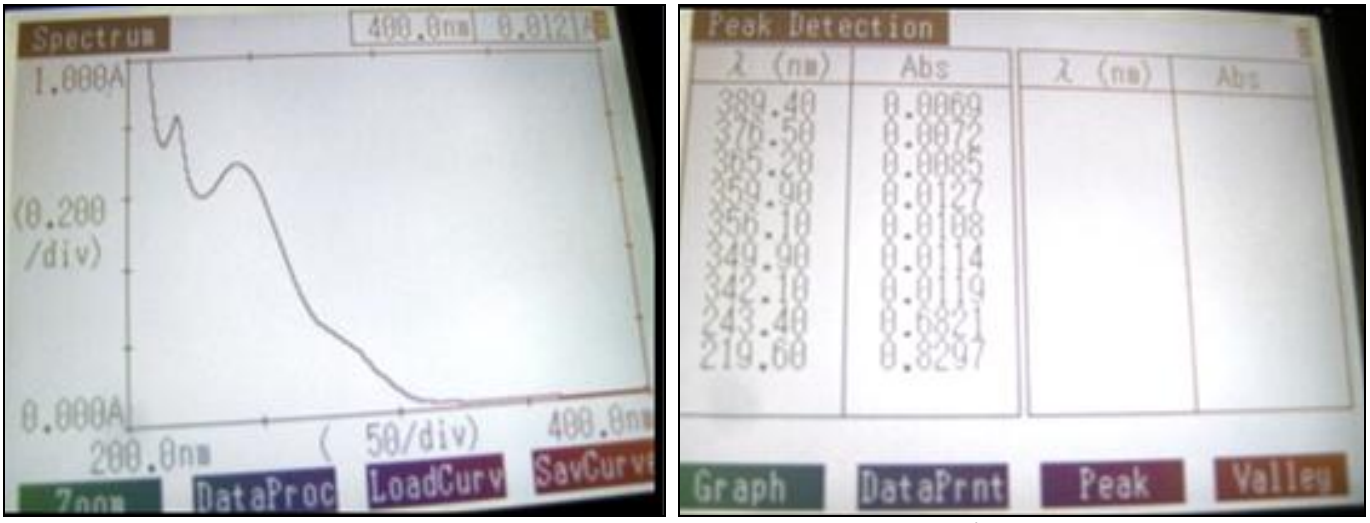


FIG. 5: SPECTRUM OF PARACETAMOL AND ITS λ_{max}

TABLE 4: STANDARD CALIBRATION CURVE CONCENTRATIONS AND ABSORBANCES.

Concentration in mcg/ml	Absorbance in nm
2	0.0356
4	0.1678
6	0.3578
8	0.4982
10	0.68211
12	0.8452

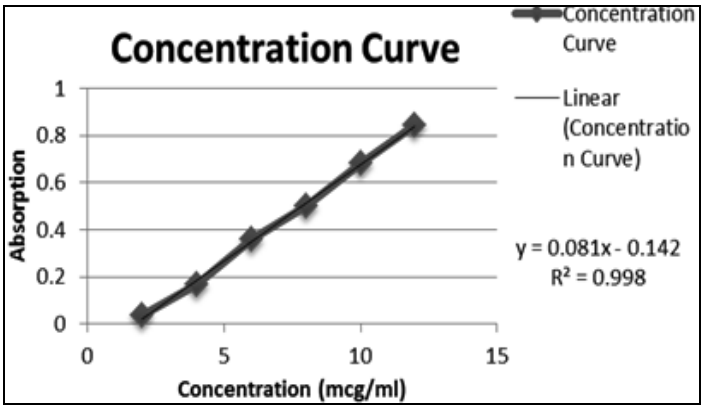


FIG. 6: CALIBRATION CURVE OF PARACETAMOL.

TABLE 5: EVALUATION OF GRANULES READY FOR COMPRESSION INTO EFFERVESCENT TABLETS

Sr. No.	Parameters	A1	A2	A3	A4	A5	A6
1	Bulk density	0.5	0.45	0.55	0.45	0.5	0.5
2	Tap density	0.714	0.625	0.714	0.714	0.655	0.645
3	Angle of Repose	27.45	30.42	26.94	29.54	27.49	26.93
4	Compressibility index	29.971	28.00	22.96	36.97	23.66	22.48
5	Hausner's ratio	1.428	1.388	1.29	1.586	1.31	1.29

TABLE 6: EVALUATION PARAMETERS OF TABLETS

STUDY PARAMETERS	F1	F2	F3	F4	F5	F6
Dimensions	14.2 ± 0.65	14.2 ± 0.45	13.9 ± 0.37	14 ± 0.33	14 ± 0.65	13.97 ±0.47
Hardness	2.63 ± 0.22	2.71 ± 0.32	2.76 ± 0.21	2.69 ± 0.3	2.71 ± 0.29	2.70 ± 0.24
Friability	0.41	0.26	0.43	0.33	0.45	0.29
% content	97.96 ± 0.31	99.25 ± 0.204	99.109 ± 0.35	99.71 ± 0.22	98.21 ± 0.24	98.79 ± 0.22
Disintegration time	62.11 ± 2.01	49.34± 1.90	35.76±2.54	37.27±2.43	35.91±1.98	33.71±2.03
Weight variation (%)	Pass	Pass	Pass	Pass	Pass	Pass

In vitro Drug Release studies:

TABLE 7: % CUMULATIVE DRUG RELEASE OF ALL THE BATCHES

TIME (Mins)	F1	F2	F3	F4	F5	F6
0	10.64	14.75	20.17	13.654	17.53	22.42
1	32.46	34.67	42.43	33.75	37.43	51.56
2	46.82	50.57	62.65	51.85	54.65	67.54
3	64.6	70.5	79.65	64.46	79.54	83.65
4	84.4	88.76	92.34	86.45	90.57	96.84
5	94.64	96.9	98.7	95.4	99.65	104.74

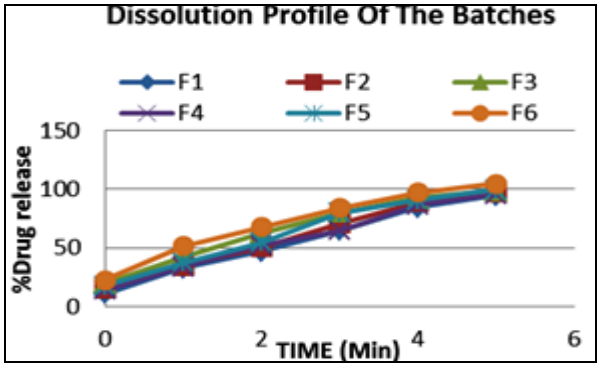
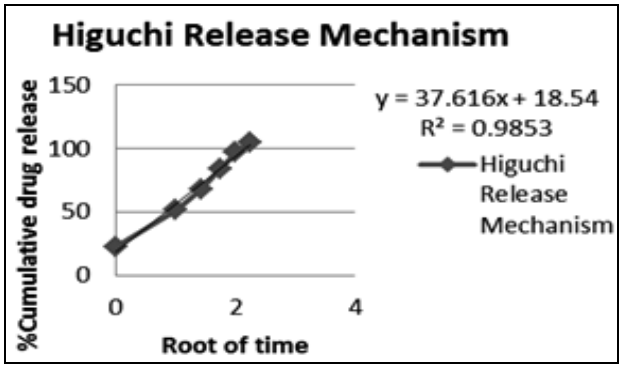


FIG. 7: DISSOLUTION PROFILE OF THE BATCHES



B

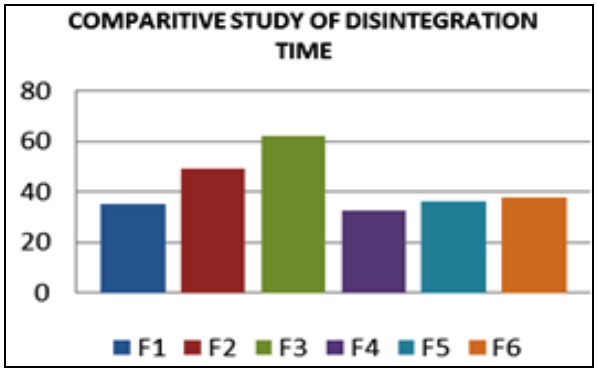
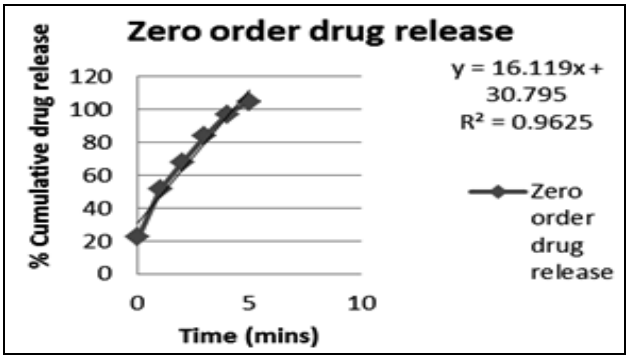
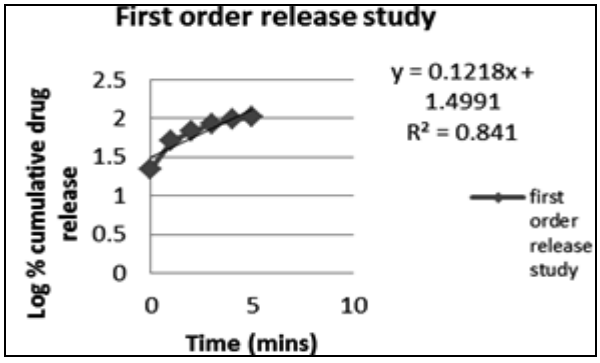


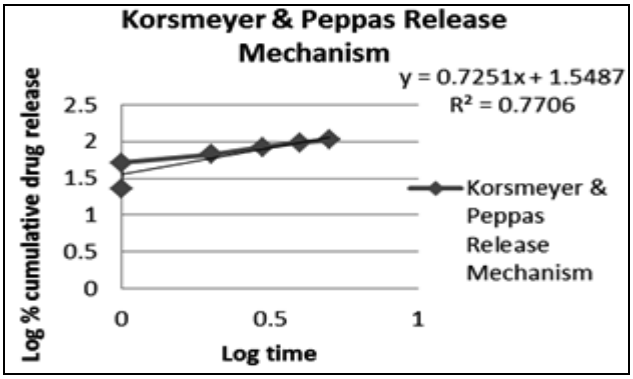
FIG. 8: STUDY OF THE DISINTEGRATION TIME



C



A



D

FIG. 9(A-D): DRUG RELEASE PROFILE STUDY

Data Analysis and Development of Polynomial Equation by Factorial design: The disintegration time data were evaluated by model dependent (curve fitting) method. Various computations for optimization study were done employing Design Expert software. Statistical second order model interaction and polynomial terms were generated for the response variable. The 3D response curve and 2D contour plot were also generated.

The equation derived for *in vitro* dispersion time of the factorial formulations is:

$$R_1 = 422.37 - 315.51X_1 - 387.63X_2 + 314.49X_1X_2$$

The negative sign of coefficients of X_1 and X_2 indicates that as the concentration of X_1 and X_2 increases the disintegration time decreases.

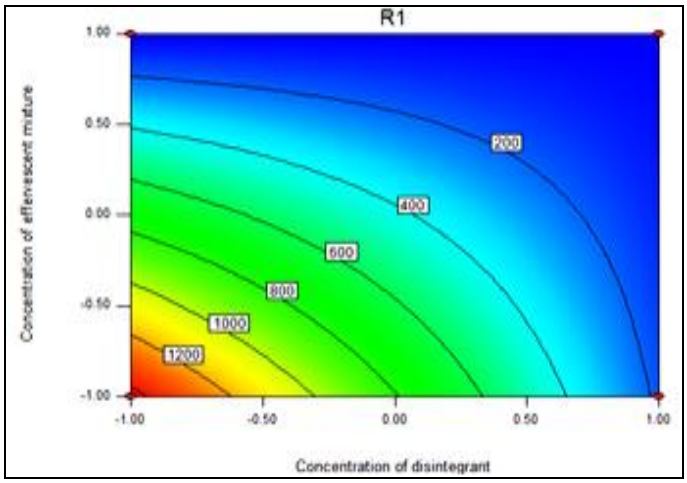


FIG. 10: CONTOUR PLOT SHOWING EFFECT OF FACTORIAL VARIABLES ON *IN VITRO* DISPERSION TIME

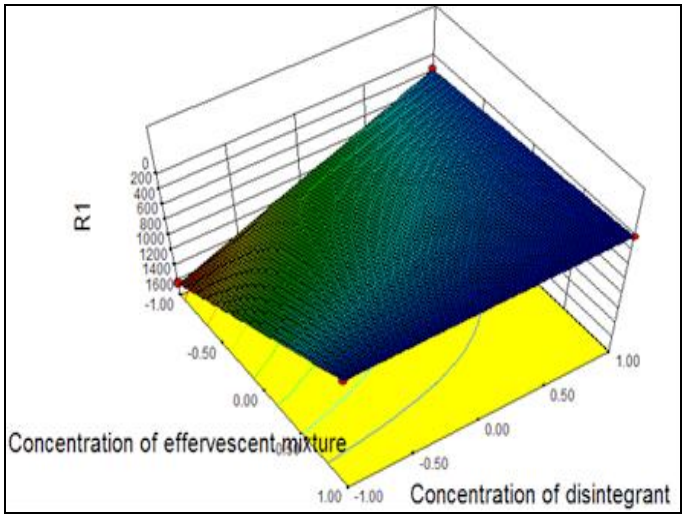


FIG. 11: RESPONSE SURFACE PLOT SHOWING EFFECT OF FACTORIAL VARIABLES ON IN VITRO DISPERSION TIME

CONCLUSION: The study was undertaken with an aim to formulate a combine effervescent tablet of Paracetamol, Aluminium hydroxide and Magnesium hydroxide.

The results of a 2^2 full factorial design revealed that the amounts of crosspovidone and effervescent material significantly affect the dependent variable, *in vitro* dispersion time. It is thus concluded that by adopting a systematic formulation approach, optimized release mechanism can be reached in the shortest time with minimum efforts.

ACKNOWLEDGMENT: The authors are thankful to the Principal Dr. Parag Gide, Dr. L.H. Hiranandani College of Pharmacy, Ulhasnagar and HSNC Board, for providing the research facilities. We are also thankful to Head, Department of Pharmaceutics, Dr. L.H. Hiranandani College of Pharmacy for giving the facilities to carry out the work.

REFERENCES:

1. Mohrle, R., in: Liberman, Lachman L. Schwartz. Pharmaceutical Dosage Form, Vol. 1, Marcel Decker Inc., New York, 2005; 285- 292.
2. G. Rajalaksmi, C.H. Vamsi, R.balachandra, N. Damodharan; "Formulation and Evaluation of diclofenac potassium effervescent tablets" in International Journal of Pharmaceutical and Biomedical research. 2011, *2*(4), 237-243.
3. K D. Tripathi; Essentials of Medical Pharmacology; 5th edition: 181-182, 594-595.
4. S.B. Shirsand, P.V. Swamy V. Kusum Devi, Sarasija Suresh: Formulation Design and Optimization of Fast Dissolving Effervescent Tablets of Clonazepam . RGUHS Journal of Pharmaceutical Sciences. Oct - Dec, 2011/ Vol 1/ Issue 3: 202 - 208**.**
5. Larry L. Augsburger and Stephan W. Hoag; Pharmaceutical Dosage Form: Tablets 3rd edition Vol. 1: 465.
6. Margadele J. O Neil, Patricia E, Heckelman, Cherie V. Koch, Kristin J. Roman et.al; "The Merk Index" 14th edition, "An Encyclopedia of Chemical, Drug and Biological"; 47.
7. K.R. Srinath, C. Pooja Chowdary, Palanisamy. P, Vamsy Krishna. A, S. Aparna1, Syed Shad Ali, P. Rakesh, K. Swetha; Formulation and evaluation of Effervescent Tablets of Paracetamol; International Journal of Pharmaceutical Research and Development May 2011; 3(3): 12; (76 - 104)**.**
8. Herbert A. Lieberman, Leon lachman and Joseph B. Schwartz; Pharmaceutical Dosage forms; Tablet, Vol. – I 2nd edition: 285.
8. Simona Bohanec, Tanja Rozman *et al.*; "Using different experimental designs in drug excipient Compatibility Studies during the Preformulation

development of a stable solid dosage formulation'; Acta Chim. Solv 2010: 57, 895-903.
9. Modi Foram. P, Patel. Priyal R; "Formulation, Optimization and evaluation of fixed dose combination of Moisture Barrier Film Coated Bilayer tablet of Artesunate and Amodiaquine Hydrochloride." International Journal of PharmTech Research Oct – Dec 2011; 3(4): 2124-2134,
10. Leon Lachman, Herbert Liberman, Joseph L. Kanig, in: Theory and Practice of Industrial Pharmacy, 2nd Edn. Varghese Publication, 1985.
11. 12. Indian Pharmacopoeia, Government of India Ministry of Health and Family Welfare. Delhi: Controller of Publications 1996; 2: 35, 448, 554.

How to cite this article:
Banerjee ND, Shukla SS and Singh SR: Formulation and evaluation of Antacid Analgesic Tablet. *Int J Pharm Sci Res* 2013; 4(6); 2327-2335. doi: 10.13040/IJPSR.0975-8232.4(6).2327-35