Journal of Applied Pharmaceutical Research
Volume 12 Issue 3, Year of Publication 2024, Page 46 – 55
DOI: https://doi.org/10.69857/joapr.v12i3.501

Check for updates

Research Article

JOURNAL OF APPLIED PHARMACEUTICAL RESEARCH | ***JOAPR***
www.japtronline.com ***ISSN: 2348 – 0335***

DESIGN AND EVALUATION OF COST-EFFECTIVE ORO-DISPERSIBLE TABLETS OF VENLAFAXINE HYDROCHLORIDE BY EFFERVESCENT METHOD

Sunita N. Mahale[1], Manisha A. Tayde[2]*, Yogita G. Ahire[3], Rupali S. Dhikale[4], Vishal S. Gulecha[3]

Article Information
Received: 29th January 2024
Revised: 12th April 2024
Accepted: 19th May 2024
Published: 30th June 2024

Keywords
Oro-dispersible tablets, Venlafaxine hydrochloride, Treated agar, Effervescent method, Directly compressible excipients

ABSTRACT
Background: Venlafaxine hydrochloride (VFH) is an antidepressant drug with poor bioavailability due to extensive first-pass metabolism. **Objective**: In the present study, oro-dispersible VFH tablets were prepared using an effervescent method to enhance patient compliance using a design of experiment (DoE) approach. **Methods**: A two-factor, three-level 3^2 full factorial design was applied to investigate the combined effect of two formulation variables: the amount of treated agar and effervescent material (mixture of sodium bicarbonate, citric acid and tartaric acid) on disintegration time and %drug release (Critical quality attributes). Treated agar (12-18%w/w) was used as a disintegrant, and a mixture of sodium bicarbonate, citric acid and tartaric acid (12-16%w/w) was used as effervescent material along with directly compressible excipients to enhance mouth feel. The association between the factors and responses was established by plotting response surfaces and contour plots. A 3D surface plot was used further to evaluate the responses to the factors. Prepared tablets were evaluated for wetting time, hardness, friability, thickness, drug content uniformity, and disintegration time. In vitro, drug release studies and stability studies were also performed. **Results**: The tablet formulation containing 17.5% w/w treated agar and 16%w/w mixture of sodium bicarbonate, citric acid and tartaric acid was found to be a promising formulation with a disintegration time of 27 seconds and in vitro drug release of 97.38% (in phosphate buffer of pH 6.8). **Conclusion**: The use of effervescent material was found to be useful for taste masking as well as patient compliance.

INTRODUCTION

The oral route is the suggested technique for giving therapeutic agents due to its accurate dosage, cost-effective therapy, self-medication, non-invasive procedure, minimum sterility limitations, flexible dosage form design, convenience of administration, and high patient compliance. The primary barrier to developing oral dose forms is their low oral bioavailability. Several factors influence oral bioavailability, including drug

[1]*Department of Pharmaceutics, Shree Panchavati Education Society's SNPT Institute of Pharmacy, Nasik, India*
[2]*Department of Pharmaceutical Chemistry, Shree Panchavati Education Society's SNPT Institute of Pharmacy, Nasik, India*
[3] *Department of Pharmacology, Shree Panchavati Education Society's SNPT Institute of Pharmacy, Nasik, India*
[4] *Department of Pharmacognosy, Shree Panchavati Education Society's SNPT Institute of Pharmacy, Nasik, India*

For Correspondence: **mtayde82@gmail.com**

permeability, aqueous solubility, dissolving rate, first-pass metabolism, presystemic metabolism, and sensitivity to efflux mechanisms [1,2]. Because fast-dissolving drug delivery systems are easy to use and increase patient compliance, they are increasingly recognised as cutting-edge medication administration techniques [3]. Taking regular tablets can be difficult in some scenarios, such as motion sickness, sudden allergic responses, coughing fits, and dehydration. Particularly younger and elderly patients who have difficulty with it. To deal with such problems, oral disintegrating or rapidly dissolving tablets have emerged as an alternative dose type [4]. Oro-dispersible tablets (ODT) are defined as a solid dosage form containing medicinal substances that disintegrate rapidly when placed upon the tongue, usually within seconds. ODTs dissolve on the tongue instantaneously, allowing the drug to disintegrate or diffuse through saliva. When a medication dissolves in solution more quickly, absorption and the onset of therapeutic actions occur more quickly [5]. When saliva moves from the mouth to the stomach, some drugs are swallowed through the mouth, throat, and oesophagus. The drug's bioavailability in these circumstances is substantially higher than in dosage forms of tablets. In both academics and business, the advantages of oral dissolving medicine formulations are increasingly recognised [6]. The key ingredient in ODT is super disintegrants, such as crospovidone, sodium starch glycolate (primogel, Explotab), etc., which allow tablets to dissolve on the tongue instantaneously and release the medication into saliva [7]. Due to oral drug absorption and pre-gastric absorption of saliva, which contains scattered drug particles and travels down into the stomach, some drugs may have a higher bioavailability. ODTs are also manufactured using a co-processed, directly compressible excipient that we developed in our labs using mannitol and native food-grade maize starch to provide a product as inexpensive as feasible [8]. Effervescent materials can be added to ODT preparation as super disintegrants. [9]. The Use of effervescent materials may provide various advantages, like improved absorption by increasing disintegration, prevention of first-pass metabolism, and increased patient compliance by masking the bitter taste of the drug [10]. Treated agar is used as a natural disintegrant and decreases disintegration time. It makes the formulation cost-effective. VFH is an antidepressant drug with poor bioavailability due to extensive first-pass metabolism [11]. To overcome first-pass metabolism and increase bioavailability and patient compliance, the project tries to formulate an orodispersible tablet of VFH along with effervescent material. The effect of effervescent material (being a super disintegrant category) and its concentration on the disintegration time of ODT was also studied. The experiment design facilitates the establishment of cause-and-effect relationships between the factors and responses by utilising statistical and scientific ideas. To maximise the output or result, the input must be controlled.

MATERIALS AND METHODS

Materials

VFH was received as a gift sample from Mega Fine Pharma Pvt. Ltd., Nashik, Maharashtra. Treated agar (TAG), sodium bicarbonate, tartaric acid, citric acid, sodium saccharin, flavour (Menthol), Talc, Sodium lauryl sulphate, directly compressible excipients (DCE), and Mannitol were procured from NDMVP's College of Pharmacy chemical store and were of analytical grade. Food-grade corn starch was procured from Manibhadra Food Products, Hubli, Karnataka, India.

Preparation of directly compressible excipients

DCE was developed in laboratories using a co-processing method and has been selected to design and evaluate cost-effective ODTs of the drug VFH. DCE was prepared using a local variety of food-grade corn starch and mannitol in a 1:1 ratio using 10% w/w starch paste for granulation. A dry and clean mortar was used to powder each ingredient, passing it through a mesh sieve of size 60 and mixing it well in a geometrical ratio. Granulating fluid and starch paste (10% w/w) were added to the powder mixture in small quantities, while thorough mixing was done after each addition to get a coherent mass. Then, it was passed through a #44 mesh sieve, and the wet granules were spread on paper and dried in a hot air oven at 55-60°C. The dried granules were passed through a #36 mesh sieve [12,13].

Preparation of treated agar

Treated agar (TAG) powders were prepared by dissolving 10 gm agar powder in 100 ml distilled water and stirring at 50 rpm with a three-bladed mechanical stirrer for 24 hrs. This leads to complete water absorption and swelling. The liquid was dried in an incubator at 37±1°C for 3 days by pouring it into a large Petri dish. It was pulverised and sifted through a #80mesh sieve [13].

Drug Excipient Compatibility

Using the potassium bromide disk technique, the drug's FTIR absorption spectra assured drug excipient compatibility [14].

Precompression studies

A physical blend of drugs and excipients was evaluated by different Precompression parameters [15].

Experimental Design

Two factors, three level (3^2) study was developed to determine the influence of selected independent variables on dependent responses using the experimental version of Design-Expert® software (design Expert -700). Two independent variables were chosen after performing preliminary trial experiments, which are as follows: concentration of TAG (A) and effervescent materials (B), and the responses measured were disintegration time (Y1) and %drug release (Y2). A trial batch showing less disintegration time was selected and considered further experimental design. Corresponding to the independent variables, three levels were established (based on the study of trial batches) as the lowest, medium and highest of the tested variables (Table 1).

Table1. Independent and Dependent variables & their levels

Factor	Level		
	Low (-)	Medium (0)	High (+)
Independent Variable	Level in (mg)		
Concentration of treated agar	25	30	35
Concentration of effervescent material	24	28	32
Dependent Variable			
Disintegration Time	Minimum		
% Drug Release	Maximum		

The matrix of 13 experimental formulations was constructed as represented in Table 2.

Preparation of ODTs

ODTs of VFH were prepared by the effervescent method (Table 3). All the ingredients were passed through the #60 mesh sieve separately. The drug and directly compressible excipient were mixed by adding a small portion of each at a time and blending it to get a uniform mixture and kept aside. To remove absorbed moisture from sodium bicarbonate and tartaric acid they were pre-heated at a temperature of 80° C for 2 hrs. and thoroughly mixed in a mortar to get a uniform powder and then added to the above blend. Then, other ingredients as per formula (Table 3) were mixed in geometrical order, except sodium lauryl sulphate and purified talc, which were added at the last and mixed for a further two minutes. The blend was compressed using 8 mm flat round punches to get tablets of 200mg weight on a 10-station rotary tablet machine (RIMEK MINI PRESS –II). A batch of 60 tablets was prepared for all the designed formulations [15,16].

Table 2: Optimisation of formulation

Run	Factor 1 (A)	Factor 2 (B)	Response 1	Response 2
1.	35	28	32	94.56
2.	30	28	35	92.04
3.	25	32	40	85.63
4.	30	28	35	92.04
5.	30	28	35	92.04
6.	25	28	45	84.67
7.	30	32	34	93.46
8.	25	24	49	82.56
9.	30	28	35	92.04
10.	**35**	**32**	**27**	**97.38**
11.	30	28	35	92.04
12.	35	24	33	93.59
13.	30	24	39	87.86

Evaluation of ODT

Weight variation

Twenty tablets were randomly selected and weighed individually. The difference between individual weight and average weight was compared to determine weight variation [17].

Hardness and friability

The Monsanto hardness tester (Pfizer tester Cadmach) and Roche friability tester (Remi Equipments) were used to determine Hardness and friability, respectively [18].

Thickness and Diameter

The tablets' thickness and diameter were determined using Vernier Calliper, and the reading was recorded in millimetres [19].

Wetting time Study

The time it took for the tablets to completely wet was measured in seconds when placed in a piece of tissue paper folded twice in a small Petri dish (internal diameter = 6.5cm) containing 5 ml of distilled water [20].

Content uniformity

Ten tablets were powdered, and a blend equivalent to 25 mg of VFH was weighed and dissolved in a suitable quantity of phosphate buffer pH 6.8. The solution was filtered through a 0.45 mm membrane filter, and drug content was analysed using a UV Spectrophotometer (UV—1700 Pharmaspec Shimadzu) at a maximum wavelength of 224 nm.

Disintegration Time

To measure the disintegration time of ODT, the tablet was placed in a Petri dish or a beaker containing 10 ml of phosphate buffer of pH 6.8 at 37°±0.5°C, and the time required for complete dispersion was determined [21].

In Vitro Drug Release Studies

The percent drug release of VFH-ODT was determined by the USP dissolution test apparatus (Lab India 2000) using the paddle method. The dissolution test was performed using 900 ml of phosphate buffer pH 6.8 at 37°±0.5°C at 50 rpm. A sample of 10 ml solution was withdrawn from the dissolution apparatus at 1, 4,7,10,13,16,19 minutes. The same quantity of sample was replaced with a fresh dissolution medium. The samples were filtered through a 0.45 µm membrane filter. The absorbance of these samples was analysed at ƛmax 224 nm. Dissolution kinetics was also studied [20].

Stability study

Short-term stability studies were conducted on the optimised formulation (F9) per the ICH guidelines (Q1AR2). The stability sample was packed in a vial and placed in the stability chamber, which had a defined storage condition of 40°C±2°C/75% RH ± 5% RH. The sample was tested at the end of the month (1 month) for Appearance, Hardness, Thickness, Drug content, and drug release percentage [21].

Statistical Analysis of Data

The data were fitted to the various models (linear, 2-FI and quadratic) and analysed by one-way analysis of variance (ANOVA). Polynomial equations explained the models and their related 3-D response surface plots were created by design-expert® software [22].

RESULTS

Drug excipient Compatibility study

The interference was verified from the FT-IR spectra, and it was found that the drug did not interfere with the excipients used. Compared with the pure VFH, the absorption peak of the spectra (Drug with excipients) showed no shift and no disappearance of characteristic peaks, suggesting no interaction between the drug and other additives (Figure 1 and Figure 2).

Table 3. Formula design for Preparation of 9 batches according to 3^2Factorial design

Name of Ingredients (mg/tablet)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8	F_9	Fc
Venlafaxine HCL	25	25	25	25	25	25	25	25	25	25
Treated Agar (TAG)	25	25	25	30	30	30	35	35	35	-
Sodium Bicarbonate	**12**	28	32	24	28	32	24	28	32	28
Citric acid+ Tartaric acid(1:1)	**6+6**									
Sodium Saccharin	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Flavour	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Talc	3	3	3	3	3	3	3	3	3	3
Sodium lauryl sulphate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
DCE	118.5	114.5	110.5	113.5	109.5	105.5	108.5	104.5	100.5	111.5
Total weight (mg)	200	200	200	200	200	200	200	200	200	200

Fc: Control formulation without treated agar; Total of 9 batches were prepared as per DoE

Evaluation of Precompression parameters:

DCE was evaluated for bulk density, tapped density, Carr's index, Hausner's ratio and hygroscopicity compared with a commercial variety of corn-starch (SD Fine Chem. Mumbai) as the control. The bulk density of pre-compression blends was found to be in the range of 0.434 to 0.560 g/cc, tapped density in the range of 0.456 to 0.650 gm/cc, the Carr's index values were in the range of 4.19 to 13.81%, Hausner's ratio in the range of 1.04 to 1.16 and angle of repose in the range of 19.22 to 29.21 indicating free-flowing properties of blend (Table 4).

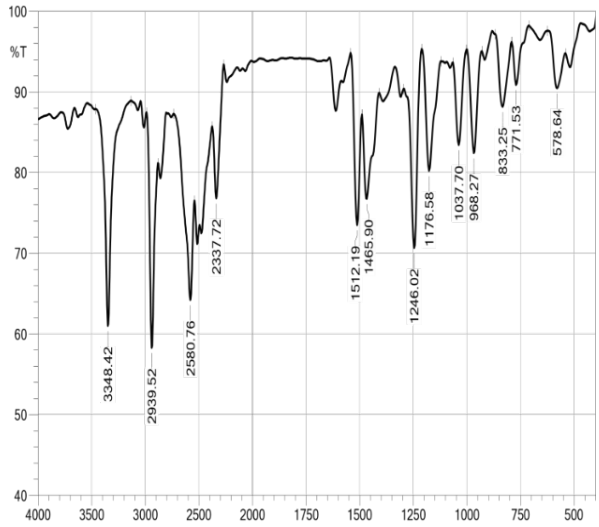

Figure 1: IR spectrum of VFH

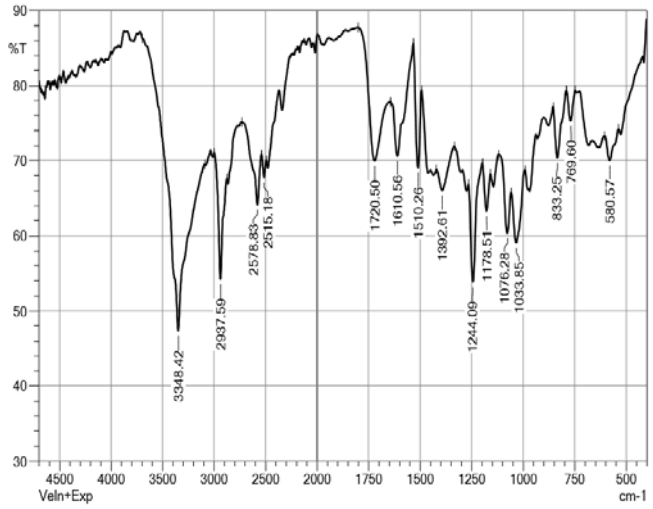

Figure 2: IR spectrum of drug and excipients

Table 4: Precompression parameters (Mean±SD)

Batch	Bulk Density gm/cm^3	Tapped Density gm/cm^3	Carr's Index %	Hausner Ratio	Angle of Repose (θ)
F_1	0.456±0.012	0.506±0.015	9.88±0.021	1.10±0.026	25.20±0.026
F_2	0.473±0.011	0.5±0.015	5.4±0.024	1.05±0.029	24.61±0.033
F_3	0.450±0.014	0.493±0.019	8.72±0.026	1.09±0.031	25.72±0.041
F_4	0.431±0.013	0.456±0.021	5.4±0.031	1.05±0.041	25.22±0.037
F_5	0.434±0.015	0.487±0.022	10.22±0.037	1.12±0.056	25.32±0.034
F_6	0.434±0.015	0.453±0.019	4.19±0.031	1.04±0.041	24.12±0.032
F_7	0.434±0.016	0.475±0.021	8.63±0.036	1.09±0.042	20.32±0.028
F_8	0.439±0.015	0.493±0.018	10.95±0.025	1.12±0.031	24.22±0.026
F_9	0.454±0.013	0.493±0.017	8.51±0.025	1.08±0.031	19.22±0.029
F_C	0.560±0.021	0.650±0.031	13.81±0.041	1.16±0.058	29.21±0.042

(SD- standard deviation), Fc –Control formulation without treated agar

Table 5: Post-compression parameters of Venlafaxine hydrochloride Oro-dispersible tablets

Batch	Hardness (Kg/cm^2)*	Friability (%)	Wetting time (Sec)*	Disintegration time (seconds)#	Weight variation (mg)*	Drug content (%) *
F_1	2.61±0.15	0.91	9	49±2.03	202±1.2	98.9±0.81
F_2	2.66±0.16	0.95	8	45±2.05	200±1.4	99.4±1.21
F_3	2.83±0.05	0.98	7	40±1.71	201±0.9	99.5±0.91
F_4	2.75±0.06	0.75	5	39±1.78	199±1.7	98.1±1.41
F_5	2.51±0.04	0.96	2	35±1.21	201±1.2	99.1±0.84
F_6	2.76±0.12	0.89	5	34±1.50	199±1.8	98.73±1.01
F_7	2.89±0.08	0.87	4	33±1.75	198±1.3	99.9±0.70
F_8	3.2±0.06	0.85	3	32±2.01	202±1.4	98.98±0.87
F_9	**3.02±0.11**	**0.71**	**2**	**27±1.95**	**200±1.2**	**100.5±0.79**
F_C	3.13±0.18	1.05	50	95±2.31	202±1.8	95.5±1.21

*n=3 ; # n = 6

Evaluation of post-compression parameters of ODTs:

ODTs of VFH were prepared using the above excipients and evaluated for post-compression parameters such as hardness, weight variation, drug content uniformity and *invitro* dispersion time (Table 5).The hardness of the tablet formulations was found to be in the range of 2.51 to 3.13 kg/cm^2. The friability values were in the range of 0.71 to 1.05. The wetting time of all formulations was found to be in the range of 2-9 seconds; for Fc, it was found to be 50 seconds. Disintegration time was found to be in the range of 27-49 seconds & for Fc it was 95 seconds (Figure 3). Weight variation was also within I.P. limits, and drug content was found to be in the range of 98.5 to 100.5%, and for Fc, it was 95.5%.

In vitro drug release study

In vitro drug release studies were performed in pH 6.8 phosphate buffer for all batches of ODTs F1, F2, F3, F4, F5, F6, F7, F8, F9, and control (Fc) without treated agar (Table 6). Findings showed that the F9 formulation released the maximum drug at 97.38%, and the Fc formulation without using agar released the least drug at 71.66% (Figure 4).

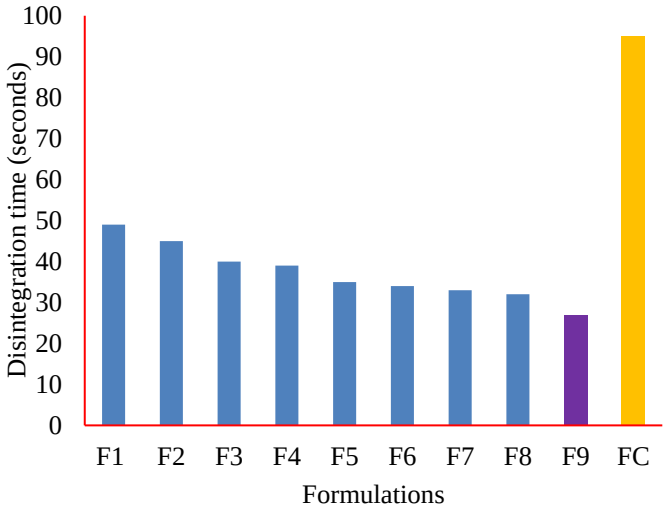

Figure 3: Graphical representation of disintegration time of all batches of ODTs

Table 6: % Drug release from ODTs

Time (min)	%Drug release									
	F_1	**F_2**	**F_3**	**F_4**	**F_5**	**F_6**	**F_7**	**F_8**	**F_9**	**Fc**
0	0	0	0	0	0	0	0	0	0	0
1	5.52±0.05	6.61±0.03	7.18±0.06	5.15±0.06	6.15±0.04	7.22±0.1	7.11±0.6	7.21±0.12	7.68±0.02	4.56±0.31
4	3.62±0.07	12.25±0.05	12.35±0.08	11.68±0.05	12.45±0.05	12.45±0.03	13.46±0.13	14.55±0.31	15.36±0.03	9.54±0.4
7	35.34±0.08	38.61±0.06	39.25±0.21	36.52±0.09	39.35±0.07	40.35±0.08	42.09±0.12	42.05±0.23	46.38±0.04	29.83±0.56
10	51.33±0.06	60.51±0.08	61.55±0.6	51.68±0.23	58.91±0.29	60.34±0.13	62.59±0.13	65.25±0.08	71.85±0.54	39.46±0.05
13	60.89±0.31	71.50±0.08	75.85±0.13	60.87±0.51	72.61±0.12	78.85±0.43	74.85±0.41	76.85±0.09	81.53±0.21	52.58±0.09
16	78.55±0.42	81.57±0.7	84.57±0.23	78.76±0.43	82.57±0.08	86.56±0.32	88.01±0.31	87.88±0.31	89.93±0.08	67.55±0.13
19	82.56±0.11	84.67±0.8	93.56±0.32	87.86±0.48	92.04±0.13	93.46±0.21	93.59±0.51	94.56±0.21	97.38±0.09	71.66±0.25

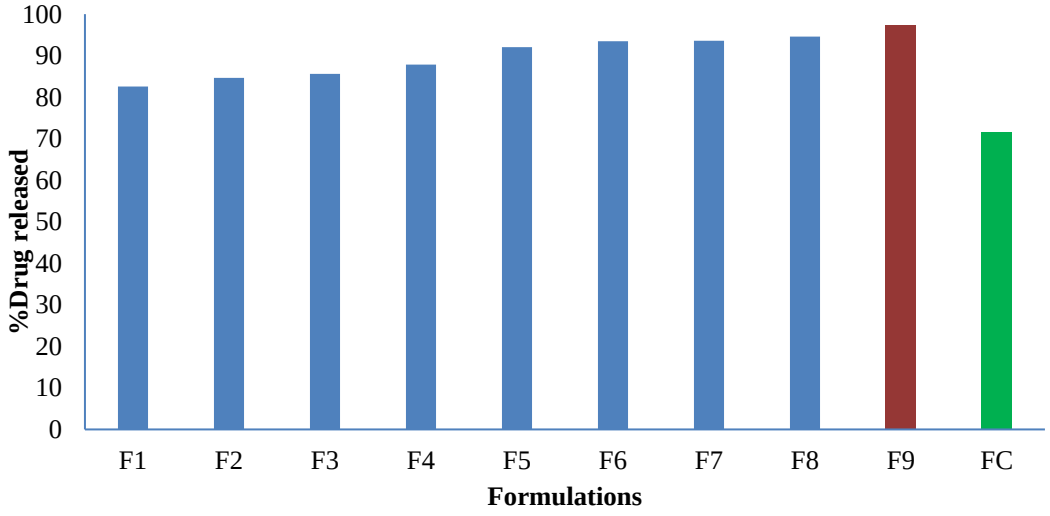

Figure 4: Graphical presentation of drug release profiles of all formulations

Data Treatment

The dissolution profile of the F9 batch was subjected to mathematical data treatment to determine its release kinetics. Five models, zero-order, first-order, Higuchi, Hixon—Crowell, and Korsmeyer–Peppas, were applied, and the data were expressed as correlation coefficients (R^2). It was found to follow the Korsmeyer Peppas model (Table 7).

Table 7: Drug release kinetics

Batch F9	**R^2**
Zero order	0.9564
First order	0.3376
Higuchi	-1.2649
Hixon – Crowell	0.7895
Korsmeyer –Peppas	0.9994

Short-term stability studies of the ODTs indicated that there are no significant changes in drug content and *in vitro* dispersion time at the end of 3 months period (Table 8).

Table 8: Result of Stability Study

Tablet Properties	**1 day**	**90 day**
General Appearance	White	White
Hardness(Kg/cm^2)	3.00	3.00
Disintegration time (Seconds)	27	29
% Drug Content	100.5	100.3
% Drug release	97.38	96.36

Statistical Analysis of Data:

ANOVA at a 95% confidence level was applied to evaluate the model's significance in the current study. A total 9 formulations were prepared for optimization of the 2 independent variables (A, B) and then characterised to analyse the influence exerted on the observed dependent responses (Y1, Y2)

Effect of Independent Variables on Disintegration Time (Y1)

Results mentioned in Table 9 showed the significance of the model. The Model F-value of 65.9 implies that the model is significant. The polynomial equation attained for this model was:

Disintegration time = +218.86782–7.66379 * A – 2.56178* B + 0.037500* AB + 0.086897*A2 + 0.01776* B2

Where, A–Concentration of TAG, B–Concentration of effervescent material

The contour plot indicates that the concentration of TAG and the concentration of effervescent material increases as disintegration time decreases. At 17.5% of TAG and 16% of effervescent material showed less disintegration time, indicated by the contour plot's blue region (Figure 5). The relationship between independent and dependent variables on disintegration time was studied by plotting the 3D response surface graphs, as shown in Figure 6.

Effect of Independent Variables on % Drug released (Y2)

The Model F-value of 76.13 implies that the model is significant. There is only a 1.92% chance that a "Model F-value" this large could occur due to noise. Values of "Prob > F" less than 0.0500 indicate that model terms are significant. B and B2 are significant model terms (Table 9).

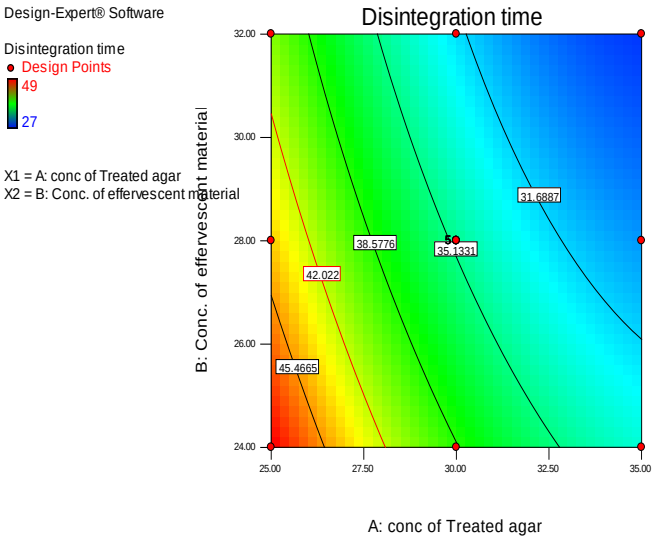

Figure 5: Contour plot disintegration time

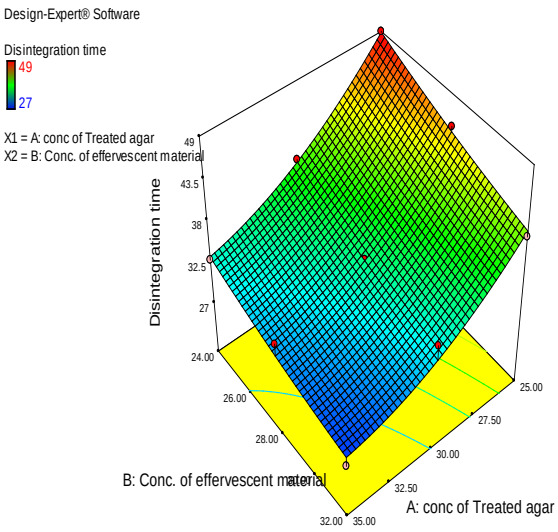

Figure 6: Surface response plot for Disintegration time

Table 9: Summary of results of quadratic model for regression analysis of responses Y1, Y2

Dependent Variables	p-value	F-ratio	Best fitted model	Lack of fit	Adequate Precision	Predicted R2	Adjusted R2	R2
Disintegration time (Y1)	**0.0001**	65.95	**Quadratic**	p>0.0001 Significant	28.369	0.7667	0.9644	0.9792
% drug release (Y2)	**0.0001**	76.13	**Quadratic**	p>0.0001 Significant	29.340	0.8416	0.9690	0.9819

The polynomial equation attained for this model was:

% CDR = -38.93253 + 4.85534* A + 2.45175*B +9.0000 * AB – 0.066972* A2- 0.039332 * B2

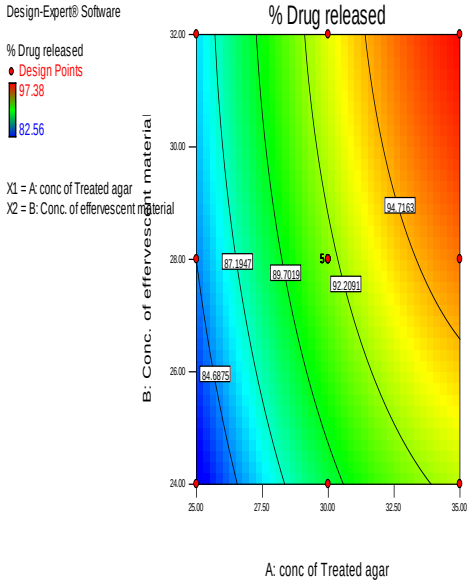

Figure 7: Contour plot for % Drug release

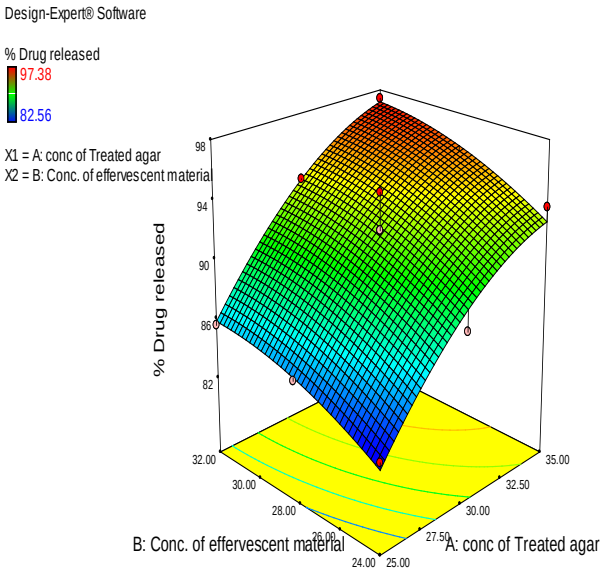

Figure 8: Surface response plot for % Drug release

Table 10: Comparative data of Composition of Batch generated by Software and its Predicted response with Experimental Batch selected

	Number	Conc of TAG	Conc of Effervescent material	Disintegration Time (seconds)	% Drug released	Desirability
Software generated	20	34.92	31.55	29.2	96.26	1.000
Experimentally selected	F9 Batch	35.00	32.00	3.02	27	97.38

The contour plot indicates that as the concentration of TAG and the concentration of effervescent material increases, the percentage of drug release increases. At 17.5 % of TAG and 16 % of effervescent material, a significant percentage of drug release was indicated by the red region of the contour plot (Figure). The relationship between independent and dependent variables on %Drug release was studied by plotting the 3D response surface graphs, as shown in Figure 8. To optimize responses Y1 and Y2, model quadratic polynomial equations were created to relate the dependent and independent variables. Ultimately, the batch that was chosen was compared using software and experimental computations, as shown in Table 10.

DISCUSSION

ODTs of VFH were prepared using an effervescent method to increase patient compliance using a design-of-experiment (DoE) approach. TAG (12-18%w/w) was used as a disintegrant, and a mixture of sodium bicarbonate, citric acid, and tartaric acid (12-16%w/w) was used as an effervescent material. Previous studies demonstrated the cost-effectiveness of using TAG for preparing ODTs. Drug excipient compatibility was evaluated. Compared with pure VFH, the absorption peak of the spectra (Drug with excipients) showed no shift and no disappearance of characteristic peaks, suggesting no interaction between the drug and other additives. Different precompression parameters

evaluated the physical blend of drug and excipients, and the powder blend before compression showed very good flow properties.

The bulk density, tapped density, Carr's index values, Hausner's ratio, and angle of repose of the blend were within range, indicating its free-flowing properties. Based on trial batches, TAG, sodium bicarbonate, tartaric acid, and citric acid were used to prepare the tablet as they showed quicker disintegration than T1 & T2. TAG and Effervescent material concentration was also selected based on trial batch T4. Post-compression parameters were also found to be within limits. The hardness of the tablet formulations was found to be desirable. The strength of a tablet plays a very important role in its marketing and dissolution. The generally agreed upper limit for friability is 1%, and all ODTs did not break or show any capping, cracking, or chipping during the test. Their friability was found within the desirable range, i.e. 0.71 to 1.05. One important metric that indicates the tablet disintegration characteristics is wetting time (WT). Faster disintegration is typically implied by shorter wetting time. The wetting time of all formulations was found to be in the range of 2-9 seconds; for Fc, it was found to be 50 seconds. Disintegration time was also within range. Weight variation was also within I.P. limits; drug content was found to be 98.5 to 100.5%, and for Fc, it was 95.5%. The formulation was optimised using 3^2 full factorial designs using design expert software.

In vitro drug release studies showed that the F9 formulation had a maximum drug release of 97.38%, and the formulation without treated agar showed less drug release of 71.66%. Contour plots indicate that as the concentration of TAG and concentration of effervescent material increases, disintegration time decreases and per cent drug release increases. 17.5% of TAG and 16% of effervescent material showed less disintegration time and significant percent drug release. The use of TAG-made formulation is not only cost-effective but also optimizes its drug release.

CONCLUSION

ODTs of VFH were successfully prepared cost-effectively using the direct compression method with treated agar. Factorial design and drug design software revealed that the concentration of treated agar and the concentration of effervescent material have a significant influence on the disintegration time and in-vitro drug release of ODT. Using an effervescent mixture further assists in taste masking and disintegration time. Undoubtedly, the availability of various technologies and the manifold advantages of ODTs will surely enhance patient compliance (with rapid onset of action, increased bioavailability, and good stability) and its popularity shortly. In vivo studies can further be assessed to correlate the findings of the study.

ACKNOWLEDGEMENTS

The authors are thankful to Megafine lab Nashik, for providing gift samples of Venlafaxine hydrochloride.

FINANCIAL ASSISTANCE

Nil

CONFLICT OF INTEREST

The authors declare no conflict of interest

AUTHOR CONTRIBUTION

Sunita Mahale and Manisha Tayde were involved in designing the study and experimental work. Yogita Ahire involved in data collection and analysis. Rupali Dhikale and V. S. Gulecha reviewed the draft of manuscript. All authors read and approved the final manuscript, confirming their agreement with the content and conclusions presented.

REFERENCES

[1] Lindgren S, Janzon L. Prevalence of swallowing complaints and clinical findings among 50-79-year-old men and women in an urban population. *Dysphagia*, **6**, 187-92 (1991).

[2] Chinwala M. Recent Formulation Advances and Therapeutic Usefulness of Orally Disintegrating Tablets (ODTs). *Pharmacy (Basel)*, **8**, 186 (2020).

[3] Kuchekar BS, Aruagam V. Fast dissolving tablets. *Indian J. Pharm.Educ*, **35**, 150 (2001).

[4] Chein YW, New York: Marcel Dekker; Oral drug delivery and delivery systems. 2nd ed. (1992).

[5] Habib W, Khankari R, Hontz J. Fast-dissolve drug delivery systems. *Crit Rev Ther Drug Carrier Syst*, **17**, 61-72 (2000).

[6] Bhushan SY, Sambhaji SP, Anant RM, Kaka Saheb RM. New drug delivery system for elderly. *Indian Drugs*, **37**, 312 (2000).

[7] Dey P, Maiti S. Orodispersible tablets: A new trend in drug delivery. *J Nat Sci Biol Med*, **1**, 2-5 (2010).

[8] Bhandari S, Mittapalli RK, Ganu R, Rao YM. Oro dispersible tablets: An overview. *Asian J. Pharm*, **2(1)**, 2 – 8 (2008).

[9] Gourichay MP, Kiaie SH, Ali N, Javadzadeh Y. Formulation and Quality control of orally disintegrating tablets (ODTs): Recent Advances and Perspectives. *Biomed Res Int*, **2021**, 6618934, (2021)

[10] Vanhere KG, Derle DV, Khatale SB, Nangude SL.A Comprehensive Review of Effervescent Tablets. *Journal of Drug Delivery and Therapeutics*, **13(7)**, 141 – 50 (2023).

[11] Bansode AS, Saravanan K. Analytical method development and estimation of venlafaxine hydrochloride in bulk and pharmaceutical dosage form by UV- Visible spectrophotometer. *International Journal of Innovative Science, Engineering & Technology*, **6(10)**, 131 – 138 (2019)

[12] Ronald P, Shashank NN, Shwetha S, Kamath K and Shabaraya AR. A Research on formulation and evaluation of fast dissolving tablets of Flunarizine HCl by sublimation method using treated agar as super disintegrant. *International Journal of Pharmaceutical and Chemical Sciences*, **3(2)**, 552 (2014).

[13] Shailaja T. Formulation and evaluation of Oro dispersible tablets of metoprolol tartrate with natural and synthetic super- disintegrants. *International Journal of Pharmacy and Pharmaceutical Sciences*, **4(3)**, 148 (2012).

[14] Wilson CG, Washington N, Peach J, Murray GR, Kennerley J. The behaviour of a fast-dissolving dosage form (Expidet) followed by g-scintigraphy. *Int.J.Pharm*, **40**, 119 (1987).

[15] Swamy PV, Shahidulla SM, Shirsand SB, Hiremath SN, Ali MY. Orodispersible tablets of carbamazepine prepared by direct compression method using 3^2 full factorial designs. *J Pharm Sci*, 7, 1 (2008).

[16] Swamy PV, Divate SP, Shirsand SB, Rajendra P. Preparation and evaluation of oro-dispersible tablets of pheniramine maleate by effervescent method. *Indian J Pharm Sci*, **71**,151 (2009).

[17] Banker GS, Anderson NR, Tablets. In: Lachman L, Liberman HA, Kanig JL, editors, The theory & practice of industrial pharmacy. Mumbai: Varghese Publishing House, 3rd ed. pp. 293 (1987).

[18] Indian Pharmacopoeia. New Delhi: Controller of Publications, Government of India, pp. 735, (1996).

[19] Sunada H, Yonezawa Y, Danjo K. Evaluation of rapidly disintegrating tablets by direct compression metho. *Drug Develop Ind Pharm*, **25**, 571–81 (1999).

[20] Radke RS, Jadhav JK, Chajeed MR. Formulation and evaluation of oro-dispersible tablets of baclofen. *Int J Chem Tech Res*, **1**, 517 (2009).

[21] Bhagwati ST, Hiremath SN, Sreenivas SA. Comparative evaluation of disintegrants by formulating cefixime dispersible tablets. *Indian J Pharm Edu Res*, **39**, 194 (2005).

[22] Kumar D, Gupta A, Mourya, Mohan M. Orodispersible tablets: an overview of formulation and technology. *World Journal of Pharmacy and Pharmaceutical Sciences*, **9(10)**, 1406 (2020).

[23] Ismail S, Khattab A. Optimization of proniosomal itraconazole formulation using Box Behken design to enhance oral bioavailability. *Journal of Drug Delivery Science and Technology*, **45**, 142 (2018).

[24] Dey P, Maiti S. Orodispesible tablets: A new trend in drug delivery. *J Nat Sci Biol Med*, **1(1)**, 2 (2010).

[25] Akihiko I, Masayasu S. Development of oral dosage form for elderly patients: Use of agar as base of rapidly disintegrating tablets. *Chem. Pharm. Bull*, **4**, 2132 (1995).

[26] Shiyani B, Gattani S, Surana S. Formulation and evaluation of bilayer tablet of metoclopramide hydrochloride and ibuprofen. *AAPS Pharm SciTech*, **9,** 818 (2008).

[27] Bhagwati ST, Hiremath SN, Sreenivas SA. Comparative evaluation of disintegrants by formulating cefixime dispersible tablets. *Indian J. Pharm. Educ*, **39(4)**, 194 (2005).

[28] Kaushik D, Dureja H, Saini TR. Formulation and evaluation of olanzapine mouth dissolving tablets by effervescent formulation approach. *Indian Drugs*, **41,** 410 (2004).

[29] Dawadi S, Pandey B, Nepal S *et al.* Formulation and evaluation of orally disintegrating tablet of metoclopramide hydrochloride *World J Curr Med Pharm Res,* **2(6)**, 322–329 (2020).

[30] Dalia A, Mahmoud HT, Adi AN, Osama B *et al* . Formulation and characterization of ODT using different co-process containing Daclatsvir: In Vitro and In Vivo pharmacokinetics study on healthy volunteers for hepatitis C treatment. *Int J App Pharm,* **14(5),** 105-112 (2022).