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FORMULATION, OPTIMIZATION, AND STANDARDIZATION OF ORODISPERSIBLE HERBAL TABLETS USING DESIGN OF EXPERIMENTS (DOE)

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ABSTRACT
Background: This study aimed to develop and optimize an orodispersible herbal tablet incorporating *Achyranthes aspera* Linn extract. Sodium Starch Glycolate and Crospovidone were employed as superdisintegrants to promote rapid tablet disintegration, while β-cyclodextrin was utilized to enhance the solubility of specific constituents within the extract. The optimized formulation exhibited a rapid disintegration time of 1.805 seconds and achieved a cumulative drug release of 98.04%, indicating improved dissolution and potential enhancement in oral bioavailability. **Methodology:** Orodispersible tablets were formulated using Design of Experiments (DOE) software, with crospovidone and sodium starch glycolate as independent variables, and time of disintegration and cumulative drug release as dependent variables. The formulation was evaluated for weight variation, uniformity, hardness, wetting time, and *in vitro* dispersion time. **Result & Discussion:** The optimized F6 batch of orodispersible herbal tablets demonstrated the following characteristics: hardness of 2.98 kg/cm², friability of 0.58%, weight variation of 3.319%, disintegration time of 13.805 seconds, wetting time of 34.4 seconds, content uniformity of 99.5%, water absorption of 36%, and cumulative drug release of 98.04%, all within the permissible limits as per official pharmacopoeialstandards. **Conclusion:** The study concludes that crospovidone and sodium starch glycolate effectively reduce disintegration time and improve cumulative drug release. These findings validate the reliability of the model, with minor deviations attributed to experimental variability.

INTRODUCTION

Orodispersible tablet formulation (ODTs) were designed to disintegrate rapidly in saliva, without the need for water. Some formulations, known as true fast-dissolving tablets, disintegrate almost instantly within seconds of being placed in the mouth. In contrast, others are classified as fast-disintegrating tablets, which contain specific agents that facilitate a quicker disintegration rate [1]. These tablets are particularly beneficial for pediatric, geriatric, and active individuals who may not have

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access to water, as well as those with difficulty swallowing due to underdeveloped muscular and nervous systems. Individuals with mental disorders, those who are uncooperative, or patients experiencing nausea may also benefit from ODTs, which provide an alternative to conventional oral dosage forms [2]. ODTs are synthesized via methods as direct compression, freeze-drying, spray drying, and sublimation. The global health-related products industry continues to expand, and it is essential to ensure the standardization of these products to guarantee uniformity and availability worldwide. Herbal medicines, renowned for their therapeutic properties, are being increasingly integrated into healthcare systems. The World Health Organization (WHO) plays a crucial role in supporting health ministries in incorporating traditional herbal medicines into healthcare, ensuring the safety of such treatments, maintaining consistent supply chains, and upholding the quality of materials [3].

The standardization of herbal medicine typically involves the use of raw materials sourced from various regions, with comparative chemical analysis performed on different batches to assess their clinical efficacy. The formulation with superior clinical outcomes is then selected. In India, the prevalence of diabetes is rising, partially due to unhealthy dietary habits, underscoring the need for more effective and standardized treatments [4]. This study aims to formulate an orodispersible tablet using the Design of Experiments (DOE) technique, aiming to achieve a tablet with sufficient mechanical integrity, rapid disintegration, and a short disintegration time when placed in the oral cavity. Diluent MCC, sodium saccharin as sweetener [5].To enhance dissolution rates and facilitate rapid disintegration, a combination of superdisintegrants, Crospovidone, and SSG, is incorporated into the tablet formulation [6].

Achyranthes aspera Linn., commonly known as "Prickly Chaff Flower," is a medicinal plant traditionally utilized in Ayurvedic medicine for the treatment of various ailments, including respiratory conditions such as asthma. Asthma is a chronic inflammatory disease of the airways, characterized by episodes of wheezing, shortness of breath, chest tightness, and coughing. The pathophysiology of asthma involves inflammation and narrowing of the air passages, leading to airflow obstruction [7]. The therapeutic potential of *Achyranthes aspera* in asthma management can be attributed to its rich phytochemical profile, which includes alkaloids, flavonoids, saponins, and terpenoids. Notably, the aqueous extract of *Achyranthes aspera* has been shown to possess significant antiallergic properties. In murine models, administration of this extract inhibited mast cell degranulation and reduced levels of Th2 cytokines, such as IL-4, IL-5, and IL-13, which are typically elevated in allergic responses. These effects collectively contribute to alleviating asthma symptoms and improving respiratory function [8]. *Achyranthes aspera exhibits* bronchodilator activity, which is essential for relieving bronchospasm associated with asthma. Studies have shown that its crude extract can inhibit bronchospasm induced by cholinergic agents in animal models, suggesting a potential mechanism for its bronchodilatory effect [9]. Incorporating *Achyranthes aspera* extract into therapeutic formulations offers a promising approach to asthma management, leveraging its multifaceted pharmacological actions to address the underlying mechanisms of the disease. This aligns with the growing interest in plant-based remedies that provide efficacy with a favorable safety profile, thereby minimizing the adverse effects commonly associated with synthetic antiasthmatic agents. *Achyranthes aspera,* traditionally used in medicine, shows promise in asthma management due to its anti-inflammatory and immune modulatory properties [10]. Animal studies suggest that its extracts reduce airway inflammation and modulate the 2-associated cytokines [11]. Phytochemicals, such as saponins and alkaloids, may contribute to bronchodilation and inhibit mast cell degranulation [12]. These actions align with conventional asthma therapies, indicating their potential as a complementary treatment.

MATERIALS AND METHODS

Plant Material Collection and Authentication

The roots of *Achyranthes aspera Linn* were collected from Maharashtra, India, for this study. To ensure the scientific rigor and reproducibility of the research, the collected plant material underwent formal authentication by the Botanical Survey of India, Pune. A specimen of the authenticated plant was subsequently deposited at the Botanical Survey of India via letter no. BSI/WRC/100-1/Tech./2019/46, dated 20/10/2019.

Excipients and Reagents

The key excipients, including Crospovidone, Sodium Starch Glycolate (SSG) & Microcrystalline Cellulose (MCC), were procured from LobaChemie Pvt Ltd. All other chemicals & reagents utilized throughout the study were of analytical reagent (AR) grade, ensuring high purity & consistency in experimental procedures.

METHODS

Extraction of *Achyranthes aspera* Root Extract

The roots of *Achyranthes aspera* Linn were selected as the specific plant part for extraction. Following harvesting, the roots were thoroughly cleaned and shade-dried to preserve their bioactive constituents. Once completely dried, they were ground into a fine powder to maximize surface area, thereby enhancing extraction efficiency. A total of 250 g of this powdered root material was subjected to Soxhlet extraction. Petroleum ether, a nonpolar solvent, was chosen to selectively extract lipophilic constituents such as sterols, terpenoids, fatty acids, and fixed oils, which have been reported in *A. aspera*. The extraction was carried out over 24 h, involving approximately eight continuous cycles of solvent percolation. After completion, the petroleum ether was evaporated under reduced pressure, and the concentrated residue was dried at room temperature to remove residual solvent, yielding a petroleum ether fraction suitable for subsequent evaluation and formulation [13].

Table 1: Characterisation and standardization of *Achyranthes aspera* extract

Extract Yield	10.5 %
Colour of Extract	Cream Colour
Physiochemical Evaluation	
Foreign organic matter	2 % w/w
Moisture Content	4 % w/w
Total ash value	4.1%
Acid-insoluble ash value	2.6 %
Water-soluble ash value	1.7%
Ethanol-soluble extractive values	9.6%
Water-soluble extractive values	6.3%

Preliminary phytochemical screening confirmed the presence of carbohydrates, proteins, steroids, terpenoids, glycosides, saponins, flavonoids, alkaloids, and tannins [14].

Figure 1: Extraction of roots of *Achyranthes aspera Linn*

PREPARATION OF TABLET

Precompression Evaluation: Angle of repose

The flow properties of the extract powder in the formulation were determined by measuring the angle of repose using the fixed-height method. A funnel with a bottom diameter of 10 mm was fixed at a height of 2 cm above a plain, smooth surface. About 10 g of the thoroughly mixed sample was slowly passed through the funnel along its wall until the tip of the formed pile touched the bottom of the funnel. A rough circle was drawn around the base of the pile, and the radius of the powder cone was measured [15].

Bulk density

The bulk densities of the powder mixture were determined by gently pouring 25 g of the sample mixture through a glass funnel into a 100 mL graduated cylinder. The initial volumes occupied by the sample were recorded [16].

Tapped density

The tapped densities (TD) of the powder mixture were determined by gently pouring 25 g of the sample mixture through a glass funnel into a 100 mL graduated cylinder. The cylinder was tapped from a height of 2 inches until a constant volume was obtained, and then the average value of all formulations was reported. The final volume occupied by the sample after tapping was recorded.

Compressibility

The compressibility of the powder mixture was calculated by comparing the bulk density and tapped density.

$$Car's\ index = \frac{Tapped\ Density - Bulk\ Density}{Tapped\ Density}\ X100$$

Hausner's ratio

It also shows densification of the herbal powder mixture, which may result from the vibration of the feed hopper, which was calculated by using the following formula [17]

$$Hausner's\ ratio = \frac{Tapped\ Density}{Bulk\ Density}$$

FTIR analysis of herbal combination

Fourier transform infrared (FTIR) spectrum of herbal extracts was subjected to determine the identification of the compound and compatibility of the drug with other excipients used in the formulation of herbal tablets [18]

Optimization of Formulations

This study aimed to develop an orodispersible tablet containing the petroleum ether extract of *Achyranthes aspera* for the management of asthma. A full factorial design was employed as the Design of Experiments (DOE) methodology to optimize the formulation. This statistical approach enabled the systematic evaluation of the effects and interactions of two independent variables namely, the concentration of superdisintegrants, on dependent responses, including disintegration time and drug

release rate. The factorial design facilitated the identification of optimal formulation parameters with a reduced number of experimental trials, thereby enhancing the efficiency of the development process. The optimized formulation exhibited a significantly reduced disintegration time, ensuring rapid drug release [19].

Experimental Design

Herbal orodispersible tablets were developed using a Design of Experiment (DOE) approach to optimize disintegration time and cumulative drug release. A total of nine formulations (F1-F9) were prepared and analyzed to determine the response outcomes of the independent variable. Selected independent variables were the amounts of Crospovidone (X1) & SSG (X2), with each variable tested at three different levels: -1, 0, and +1. The table below gives details levels of independent variables and full factorial design [20]

Table 2: Independent variable Design

Factor	Level used, actual (coded)		
Independent Variables	**Low (-1)**	**Medium (0)**	**High (+1)**
X1 (mg)	30	35	40
X2 (mg)	5	10	15

The above table shows the actual and coded levels of Crospovidone (X1) and Sodium Starch Glycolate (SSG) (X2) used in the factorial design. These levels were selected based on literature reports confirming their effectiveness as superdisintegrants. The chosen ranges (30–40 mg for Crospovidone and 5–15 mg for SSG) significantly affect disintegration time and drug release without compromising tablet integrity. The design enables assessment of both individual and interactive effects to optimize the formulation efficiently.

Procedure

Nine orodispersible herbal tablet formulations (F1 to F9) were prepared using direct compression, incorporating varying excipient concentrations based on a factorial design. Solid ingredients were weighed, ground in a porcelain mortar, and then sieved through a 60-mesh screen to ensure uniformity. The petroleum ether extract of *Achyranthes aspera* was complexed with β-cyclodextrin using the kneading method, where a 1:1 ratio of extract and β-cyclodextrin was triturated with 50% ethanol to form a paste. This was kneaded for 45 minutes, dried at 40°C, pulverized, and sieved. The complex was then blended with super-disintegrants Crospovidone and SSG using geometric dilution in a polyethylene pouch to ensure uniformity. The final blend was compressed into 400 mg tablets using a Cadmach CM-1 single-punch machine with 9 mm round, flat-faced punches. The compression force was adjusted for optimal tablet hardness. All formulations (F1–F9) were evaluated for quality control parameters, including hardness, friability, weight variation, disintegration time, and in vitro drug release. Crospovidone and SSG concentrations were used as independent variables in a full factorial design for optimizing disintegration time and drug release [21].

Table 3: Formulation table of fast-disintegrating tablets of *Achyranthes aspera* root extract

Ingredients (mg/tablet)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Extract of DI	200	200	200	200	200	200	200	200	200
B-cyclodextrin	100	100	100	100	100	100	100	100	100
Crospovidone	30	30	30	35	35	35	40	40	40
Sodium starch glycolate	5	10	15	5	10	15	5	10	15
Microcrystalline cellulose	20	20	20	20	20	20	20	20	20
Sodium saccharin	15	15	15	15	15	15	15	15	15
Lactose(Balancing)	20	15	10	15	10	05	10	5	10
Magnesium stearate	5	5	5	5	5	5	5	5	5
Talc	5	5	5	5	5	5	5	5	5

FORMULATION EVALUATION

Weight Variation

The weight variation of tablets was carried out to ensure that each tablet contains the proper amount of drug. The test was performed by weighing 20 tablets individually using an analytical balance, then calculating the average weight and comparing the individual tablet weights [22].

Hardness

The conformation of tablets for capping, abrasion, or breakage under storage conditions, transportation, and handling before use

depends on tablet hardness (kg/cm^2). The tablet was placed between two anvils; the force applied to the anvils and the crushing strength required to break the tablet were recorded. The crushing strength test was performed on 20 tablets of each formulation.

Friability

Friability was assessed using the Roche Friabilator, expressed as a percentage. Initially, the weight of each tablet is recorded individually (W-initial). The formulation was then placed in a chamber rotating at 24 rpm, subjecting the tablets to a drop at a height of 4 inches for approximately 100 cycles. After this process, the tablets are weighed again (W final) to observe any weight loss. The acceptable limit for weight loss is between 0.4% and 1% of the initial tablet weight [23]

Water absorption ratio

A piece of tissue paper folded twice was placed in a Petri dish (internal diameter, 5.5cm) containing 6 mL of purified water. The tablet was placed on the tissue paper and allowed to become thoroughly wet. The wetted tablet was removed and reweighted.

Wetting Time

A two-fold tissue paper was placed in a Petri dish containing 10 mL of water, which was mixed with a few drops of Eosin dye for visual clarity. The formulation was placed on top of the tissue paper, and the time it took for the water to reach the upper surface of the tablet was recorded as the wetting time [24]

Disintegration Time

The disintegration time of the tablets was tested using water at 37 ± 0.4°C to simulate physiological conditions. Six tablets were placed one by one in the disintegration apparatus, and the time each tablet took to disintegrate completely, leaving only insoluble fragments, was recorded. The average disintegration time of the six tablets was then calculated.

Drug Content

Twenty tablets, each containing 200 mg of petroleum-ether extract (API), were powdered, and a portion equivalent to 240 mg of extract was transferred into a 400 mL volumetric flask. The extract was dissolved in 300 mL of 0.1 N HCl with vigorous shaking, diluted to volume, and filtered. An aliquot of 10 mL of the filtrate was further diluted to 100 mL with distilled water. Absorbance was recorded at 207 nm, and a calibration curve (10–50 µg/mL) was constructed. Drug content was calculated from the calibration curve; tests were performed in triplicate [25]

Cumulative Drug Release

The in vitro drug release of the tablets was studied using a USP Type II apparatus (paddle method). A phosphate buffer (pH 6.8) was used as the dissolution medium and maintained at 37 ± 0.5°C with continuous stirring. Tablets were placed in the vessel, and at fixed time intervals, 5 mL of the medium was withdrawn and replaced with fresh buffer to maintain sink conditions. The collected samples were filtered and analyzed spectrophotometrically at 207nm to measure drug concentration. The cumulative percentage of drug released was calculated and plotted against time to obtain the drug release profile. The experiment was conducted in triplicate for each formulation to ensure accuracy and reproducibility [26]

RESULT AND DISCUSSION

The comprehensive evaluation of pre-compression and post-compression for all nine orodispersible herbal tablet formulations (F1-F9) is presented in Tables 4 and 5. This table serves as a central repository for the experimental results of all quality control parameters, enabling direct comparison across formulations and facilitating the identification of trends that led to the selection of the optimized batch. The data provides empirical evidence supporting claims about tablet performance.

Compatibility studies (extract–excipients)

FT-IR analysis was performed on the pure extract and the pure extract with excipients to study functional group frequencies and compatibility. The pure extract showed peaks at 3392.43, 3008.45, 2928.83, 2859.05, 2828.03, 1740.38, 1615.13, 1410.81, 1230.86, 1062.77, and 931.42 cm^{-1}, while the extract with excipients exhibited peaks at 3378.40, 2976.59, 2879.56, 2824.13, 1719.50, 1618.58, 1402.30, 1241.13, 1036.01, and 990.70 cm^{-1}. No new peaks appeared, confirming compatibility.

Drug Content Assay

The calibration curve of the petroleum-ether extract showed excellent linearity (10–50 µg/mL) with the regression equation $y = 0.045x + 0.0046$($R^2 = 0.9999$). Drug content in tablet batches ranged from 93.48% to 99.5%, indicating uniform distribution of the extract. Batch F6 showed the highest content (99.5 ± 0.027%), while F1 recorded the lowest (93.4 ± 0.020%). The results confirm the assay to be reproducible and reliable.

Table 4: Pre-Compression evaluation of Fast Disintegrating Herbal Tablet of *Achyranthes aspera* Root Extract

Batch	Bulk density (gm/ml)	Tapped density (gm/ml)	Car's index	Hausner ratio	Angle of Repose
F1	0.407± 0.012	0.532±0.007	23.50 ± 2.00	1.307 ± 0.045	26.150±1.538
F2	0.417±0.025	0.541±0.013	22.92 ± 2.13	1.297 ± 0.037	27.167±1.363
F3	0.347±0.029	0.503±0.013	31.01 ± 1.89	1.450 ± 0.017	22.487±0.788
F4	0.437±0.017	0.547±0.021	20.11 ± 1.90	1.252 ± 0.119	27.823±1.253
F5	0.407±0.017	0.569±0.002	28.47 ± 1.99	1.398 ± 0.054	26.807±1.814
F6	0.447±0.029	0.580±0.030	22.93 ± 1.70	1.297 ± 0.040	29.224±2.455
F7	0.427±0.045	0.573±0.009	25.48 ± 1.85	1.342 ± 0.037	27.691±1.456
F8	0.393±0.012	0.601±0.025	34.61 ± 1.63	1.530 ± 0.084	27.757±2.101
F9	0.437±0.012	0.554±0.031	21.12 ± 1.96	1.268 ± 0.075	27.692±1.137

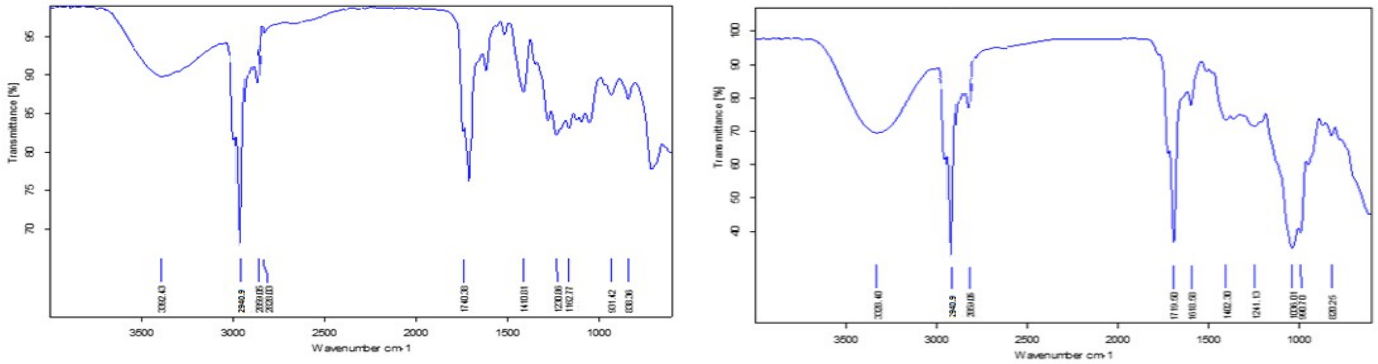

Figure 2: AFTIR Spectra of Pure extract and Pure extract with Excipients

Table 5: Evaluation of Fast Disintegrating Herbal Tablet of *Achyranthes aspera* Root Extract

Batch	Hardness	Friability (%)	Weight Variation (%)	Disintegration Time (sec)	Wetting time (sec)	Drug Content (%)	Water absorption ratio(%)
F1	2.99±0.016	0.558±0.016	4.467±0.024	17.132±0.030	69.8±1.04	93.438±0.020	26 ± 1.12
F2	2.94±0.075	0.338±0.017	3.447±0.096	15.579±0.067	39.0±0.95	97.527±0.094	28 ± 1.34
F3	2.96±0.016	0.548±0.240	3.396±0.022	14.811±0.098	42.4±1.15	97.875±0.097	29 ± 1.40
F4	3.13±0.18	0.911±0.019	3.41±0.098	18.791±0.065	89.0±0.85	97.489±0.098	30 ± 1.20
F5	2.98±0.05	0.954±0.026	3.499±0.064	15.238±0.239	66.0±1.35	97.451±0.065	32 ± 1.09
F6	2.98±0.024	0.58±0.098	3.319±0.067	13.805±0.027	34.4±1.48	99.5±0.027	36 ± 1.59
F7	3.14±0.18	0.98±0.022	0.974±0.243	19.072±0.101	67.8±0.35	99.353±0.019	43 ± 2.01
F8	3.06±0.06	0.55±0.066	2.431±0.023	16.909±0.249	41.7±1.45	97.905±0.249	45 ± 2.06
F9	2.96±0.004	0.75±0.242	4.51±0.236	14.123±0.096	29.1±1.05	96.394±0.032	48 ± 2.46

Data are represented as mean±SD (n=3)

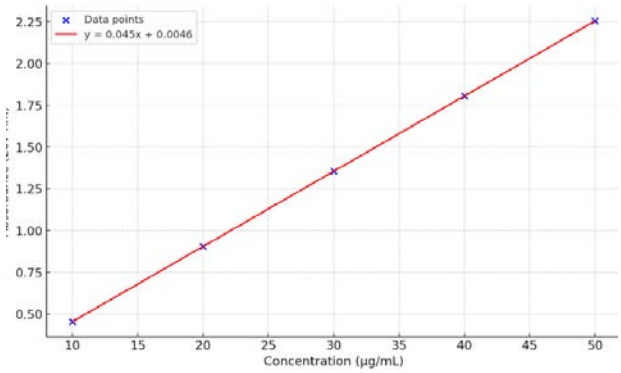

Figure 3:A calibration curve of Petroleum ether extract tablet

Characteristics of the Optimized F6 Batch

The optimized F6 batch of orodispersible herbal tablets demonstrated a favorable profile across pre-compression and post-compression parameters. In terms of pre-compression, it exhibited excellent flow and compressibility characteristics with a bulk density of 0.447 g/ml, a tapped density of 0.580 g/ml, a Carr's index of 9.66% (indicating excellent compressibility), Hausner ratio of 0.96 (reflecting superior packing), and an angle of repose of 29.22° (suggesting good flowability). These properties ensured uniform die filling & consistent tablet weight.

Post-compression evaluation of the F6 batch exhibited a hardness of 2.98 kg/cm², friability of 0.58%, weight variation of 3.319%, disintegration time of 1.805 seconds, and wetting time of 34.4 seconds. The drug content was high at 99.5%, with a water absorption ratio of 36%. The most significant performance indicator, cumulative drug release, achieved 98.04%, establishing F6 as the optimized formulation. The dissolution study, performed using phosphate buffer pH 6.8, revealed excellent drug release characteristics across the formulations. Notably, more than 70% of the drug was released within 10 minutes by most batches. Specific comparisons highlight the effectiveness of the optimized formulation. Batch F-1, F-4, and F-7, which contained 3% superdisintegrants, released 81.29%, 86.23%, and 94.93% of the drug, respectively, by 12 minutes. Among all prepared batches, the F6 batch demonstrated the highest cumulative drug release, achieving 98.04% by 12 minutes. This rapid and high cumulative drug release is critical for ODTs, as it directly impacts the potential for fast absorption and onset of therapeutic action. The dissolution kinetics for all formulations over time are presented in Figure 4.

The statistical analysis, including regression analysis and ANOVA, provided robust validation for the Design of Experiments models. All polynomial equations derived from the analysis were found to be statistically significant ($P<0.001$), confirming that the independent variables had a measurable and non-random effect on the measured responses. The model fit statistics, presented in Table 6, further underscore the reliability and predictive accuracy of the statistical models.

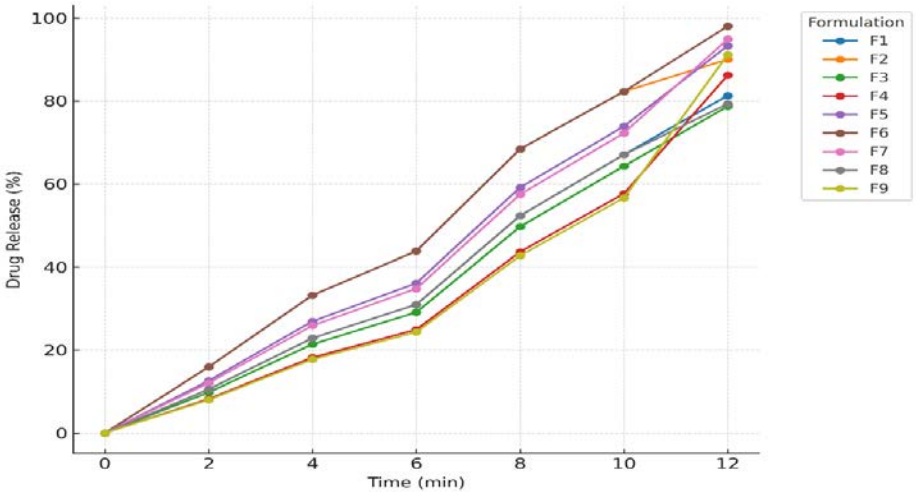

Figure 4: Drug release (%) of formulations versus time (min)

Table 6: Fit Statistics Showing R² Response Values

Response	F Value	P Value	R²	Adjusted R²	Predicted R²
R1: Weight Variation (%)	18.45	0.0001	0.9912	0.9856	0.9820
R2: Disintegration time (sec)	22.36	0.0001	0.9934	0.9889	0.9860
R3: Wetting time (sec)	164.25	0.0001	0.9987	0.9978	0.9965
R4: Content Uniformity (%)	15.72	0.0001	0.9876	0.9810	0.9785

The high R² values (0.9876–0.9987) indicate that the models explain nearly all the variance in the measured responses, confirming the robustness of the chosen formulation factors. The predicted R² values were in close agreement with the adjusted R² values, showing the models have strong predictive capability and are not overfitted. The regression analysis provided

mechanistic insights into the individual and interactive effects of the superdisintegrants: Crospovidone (X1). When used in higher amounts, the tablets performed poorly. The tablets took longer to break down and get wet, showed more variation in weight, and had less uniform drug content. This may happen because too much Crospovidone can form a gel and block water entry. Sodium Starch Glycolate (X2 worked well as expected. Higher amounts helped the tablets break down and get wet faster. The study showed that using too much of either disintegrant reduced their usefulness. Very high levels can cause saturation or gel formation, which makes them less effective.

$$Weight\ Variation\ (\%) = 2.10 - 0.48A + 0.42B + 0.35AB + 0.29A^2 + 0.38B^2$$

$$Disintegration\ Time\ (s) = 15.23 + 1.15A - 1.32B + 0.54A^2 + 0.26B^2$$

$$Wetting\ Time\ (s) = 68.45 + 2.10A - 3.25B + 0.89A^2 + 0.72B^2$$

$$Content\ Uniformity\ (\%) = 98.12 - 0.35A + 0.22B - 0.18AB - 0.15A^2 - 0.10B$$

This analysis highlights the importance of optimizing the balance between Crospovidone and SSG to achieve fast disintegration and wetting while maintaining uniformity and weight consistency. Response surface plots (Figures 5–8) further illustrate the interactions between factors and responses.

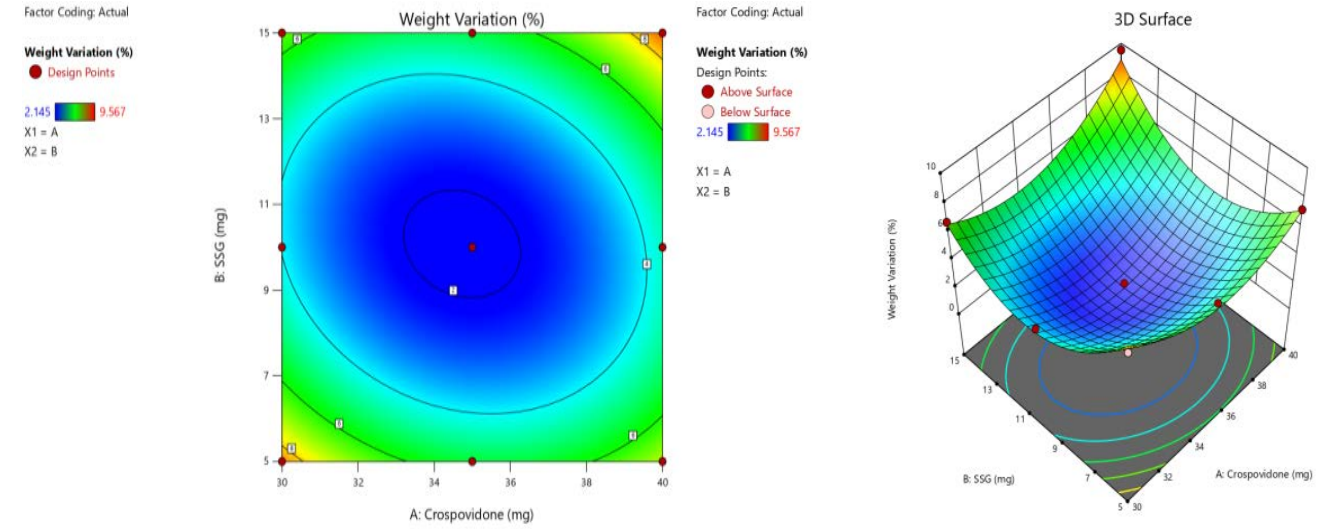

Figure 5: Response surface plot showing the effect of Crospovidone and Sodium Starch Glycolate (SSG) concentrations on the Weight Variation of orodispersible herbal tablet

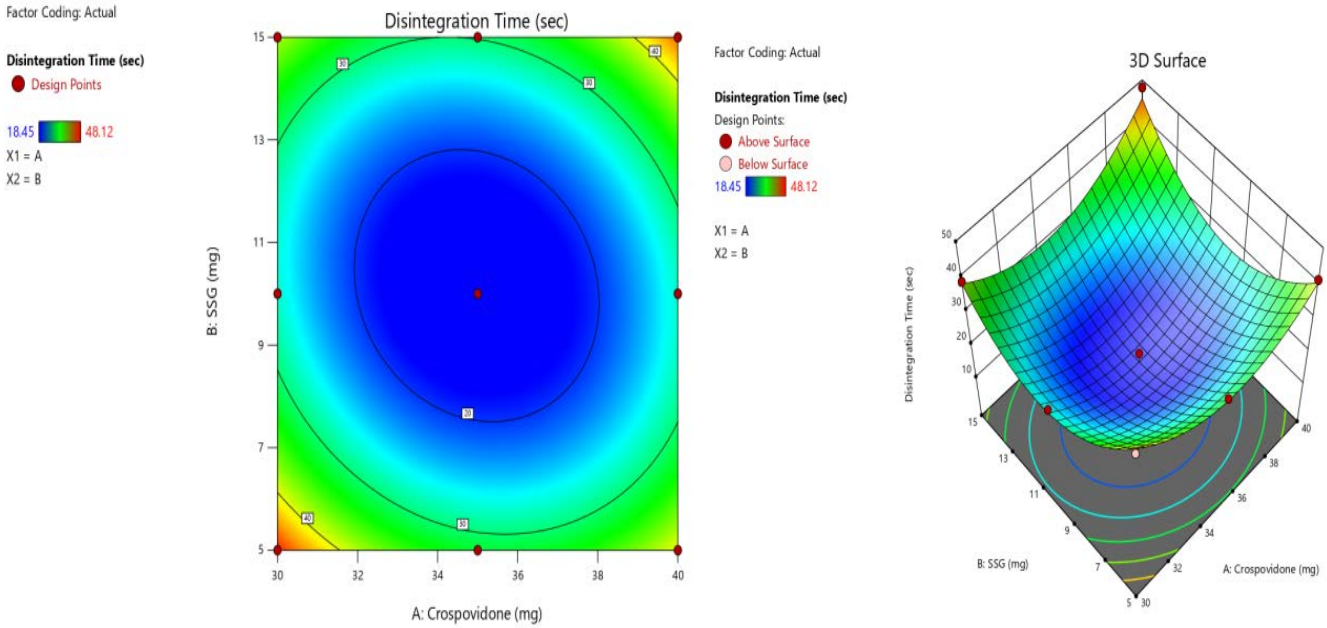

Figure 6: Response surface plot showing the effect of Crospovidone and SSG concentrations on the Disintegration Time (Seconds) of orodispersible herbal tablets.

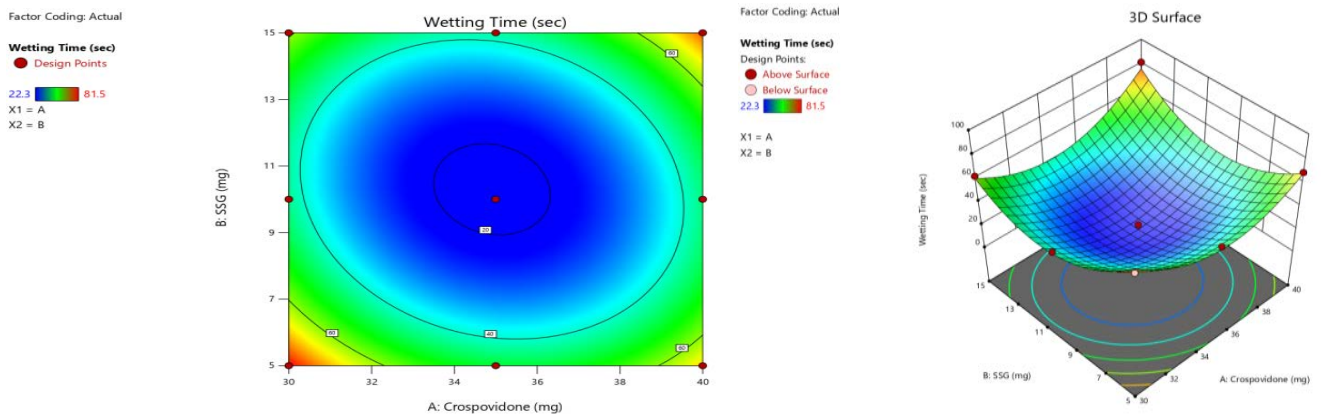

Figure 7: Response surface plot showing the effect of Crospovidone and SSG concentrations on the wetting time of orodispersible herbal tablets

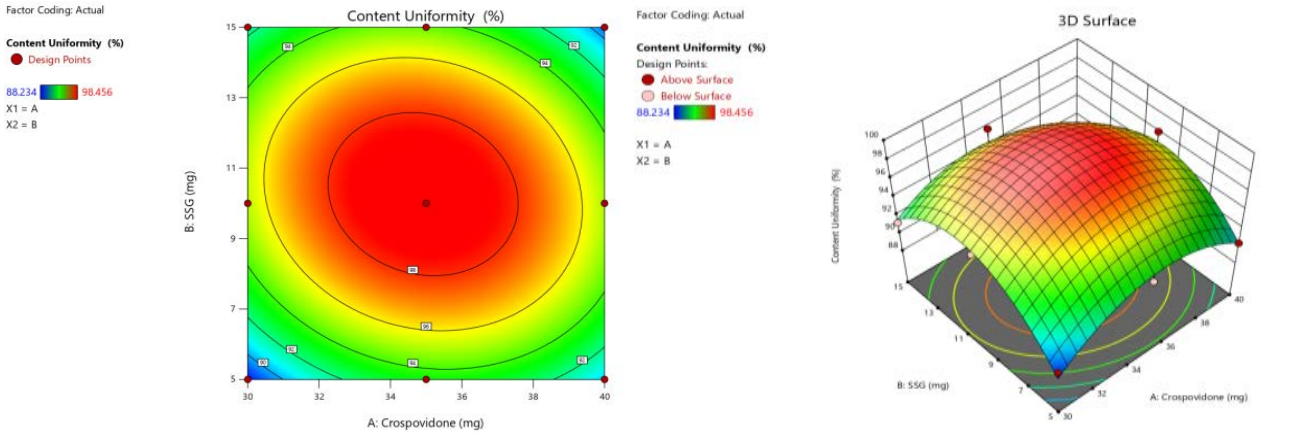

Figure 8: Response surface plot showing the effect of Crospovidone and SSG concentrations on the Content Uniformity (%) of orodispersible herbal tablets

CONCLUSION

The study successfully developed and optimized an orodispersible herbal tablet formulation incorporating *Achyranthes aspera Linn* extract through a rigorous DOE approach. The optimized formulation, specifically the F6 batch containing 35 mg of Crospovidone and 15 mg of Sodium Starch Glycolate (SSG), demonstrated excellent disintegration efficiency, achieving a rapid disintegration time of 13.805 seconds. This formulation also exhibited enhanced cumulative drug release, reaching 98.04%, which is a crucial characteristic for the rapid onset of action and improved bioavailability. The formulation successfully met key pharmacopoeial standards & the statistical analysis confirmed strong correlations ($P<0.001$) between excipient conc. & critical performance attributes such as disintegration time, dispersion time & content uniformity. This validation underscores the robustness and reliability of the DOE optimization methodology employed. The synergistic action of Crospovidone and SSG as superdisintegrants was instrumental in enabling rapid tablet breakdown and improved drug release. This rapid disintegration and enhanced drug release are essential features for patient populations facing swallowing difficulties, including pediatric and geriatric patients, directly contributing to improved oral drug bioavailability and patient compliance. The technical achievements of this research thus translate directly into tangible benefits for patient care, emphasizing the real-world impact of the developed formulation.

FINANCIAL ASSISTANCE

NIL

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHOR CONTRIBUTION

Ganesh Shinde, Ravindra Jadhav, and Rahul Godge contributed to planning, conceptualization, data collection, and paper

writing. Datta Prasad Vikhe, Vishal Tambe, and Shubham Khule contributed to data collection, literature review, and data interpretation. All authors contributed to the completion of the manuscript.

REFERENCE

[1] Ghourichay MP, Kiaie SH, Nokhodchi A, Javadzadeh Y. Formulation and Quality Control of Orally Disintegrating Tablets (ODTs), Recent Advances and Perspectives. *Biomed Res Int,***7(1)**, 51-58 (2021) https://doi.org/10.1155/2021/6618934.

[2] Chinwala M. Recent Formulation Advances and Therapeutic Usefulness of Orally Disintegrating Tablets (ODTs). *Pharmacy (Basel),* **8(4),** 186 (2020) https://doi.org/10.3390/pharmacy8040186.

[3] Kumar D, Kumar A, Malik J, Semwal P. Formulation and Evaluation of Fast Dissolving Tablets Uncoated Tablets of Drotaverine HCL. *World Journal of Pharmaceutical Research,* **9(1),** 1716-1727 (2020) https://doi.org/10.20959/wjpps20201-16560

[4] Kharade SB, Bais SK. Review on Quality Aspects of Herbal Drugs and its Formulations. *Internationl journal of Advanced Research in Science Communication and Technology,* **3(4),** 161-175 (2023) https://doi.org/10.18231/j.joapr.2024.12.2.124.130.

[5] Sharma S, Shikha B. A review: An overview of Natural superdisintegrants Research. *Journal of Topical and Cosmetic Sciences,* **12(1)**, 13-24 (2021) https://doi.org/10.52711/2321-5844.2021.00003.

[6] Mahale S, Tayde M.Design and evaluation of cost-effective oro-dispersible tablets of venlafaxine hydrochloride by effervescent method. *Journal of Applied Pharmaceutical Research, **12**(3),* 46-55 (2024) https://doi.org/10.69857/joapr.v12i3.501.

[7] Gosavi OR. Exploring the therapeutic potential of *Achyranthes aspera*: A comprehensive review. *WJBPHS,*18(2), 239-245 (2024) https://doi.org/10.30574/wjbphs.2024.18.2.0230.

[8] Paula A, Todoran N. Development and Evaluation of Cannabidiol Orodispersible Tablets Using a 2^3-Factorial Design. *Pharmaceutics,* **14(7),** 1467 (2022) https://doi.org/10.3390/pharmaceutics14071467

[9] Kaushik A. Protective effect of *Achyranthes aspera* against compound 48/80, histamine and ovalbumin-induced allergic disorders in murine model. *Molecular Biology Reports,* 51(1), 202 (2024) https://doi.org/10.1007/s11033-023-09137-2.

[10] Kumar A, Shukla AK. Evaluation of anti-asthmatic activity of *Achyranthes aspera* in ovalbumin-induced murine model,*Molecular Biology Reports,* **51(1),** 89–98(2024) https://doi.org/10.1007/s11033-023-09137-2

[11] Sharma R. Modulatory effects of *Achyranthes aspera* extract on Th2 cytokines in allergic airway inflammation: An experimental study, *J Ethnopharmacol*, **305**, 116058 (2023) https://doi.org/10.1016/j.jep.2022.116058.

[12] Patel Patel M, Sutar N, Goyal R. Phytochemical screening and bronchodilatory potential of *Achyranthes aspera*: Implications for asthma treatment, *Pharmacogn Rev*, **6(32)**, 99–106. (2022) https://doi.org/10.4103/phrev.phrev_32_21

[13] Shinde G, Kunkulol R. Evaluation of Anti-asthmatic activity of *Achyranthes aspera* Linn root Extract. *Research Journal of Pharmacy and Technology,* **16(5),** 2287-0 (2023) https://doi.org/10.52711/0974-360X.2023.00375.

[14] Bhat LR, Vora AT, Damle MC. Simultaneous estimation of nebivolol hydrochloride and amlodipine besylate in bulk and combined tablet dosage form by ultraviolet spectrophotometry. *Indian Drugs,* **44(12)**, 915-919 (2007) https://doi.org/10.53879/id.62.01.149965

[15] Kumar D, Kumar A, Malik J, Semwal P. Formulation and Evaluation of Fast Dissolving Uncoated Tablets of Drotaverine HCL. *World Journal of Pharmaceutical Research*, **9(1)**, 1716-1727 (2020) https://doi.org/10.20959/wjpps20201-16560

[16] Jadhav N, Jadhav R, Jadhav S, Jadhav R. Formulation and Evaluation of Herbal Tablets Containing Extract of Trigonella foenum-graecum Linn. *International Journal of Pharmaceutical Sciences and Research*, **12(7)**, 3880-3888 (2021). https://doi.org/10.13040/IJPSR.0975-8232.12(7).3880-88

[17] Chaudhari S, Bhalerao K, Nandgude T. Formulation and Evaluation of Herbal Tablets Containing Ethanolic Extract of Terminalia chebula Retz. *Journal of Drug Delivery and Therapeutics*, **10(6-s)**, 190-195 (2020). https://doi.org/10.22270/jddt.v10i6-s.4360

[18] Patel R, Patel M, Patel H, Suthar M. Preformulation Studies and Formulation Development of Herbal Tablet Containing Aegle marmelos. *International Journal of Pharmaceutical Sciences Review and Research*, **64(1)**, 24-30 (2020) https://doi.org/10.47583/ijpsrr.2020.v64i01.005

[19] Patil DJ, Jahagirdar SN, Mandhare SB. Validated Stability Indicating RP-HPLC Method for the Quantification of Process Related Impurities of Solifenacin and Mirabegron in Pharmaceutical Formulations. *International Journal of Drug Delivery Technology*,**14(1)**, 55-60 (2024) https://doi.org/10.25258/ijddt.14.1.10

[20] Dawadi S, Pandey B, Nepal S. Formulation and evaluation of orally disintegrating tablet of metoclopramide hydrochloride. *World J Curr Med Pharm Res,* **2(6),** 322–329 (2020) https://doi.org/10.37022/wjcmpr.vi.162.

[21] Vanhere KA. Comprehensive Review of Effervescent Tablets. *Journal of Drug Delivery and Therapeutics*, **13(7)**, 141 – 50 (2023) https://doi.org/10.22270/jddt.v13i7.6120.

[22] Channi NM, Hurkadale PJ, Bolmal UB, Bidikar CM.Formulation Design and Optimization of Poly-Herbal Chewable Tablets Using

JMP Tool. *Pharmacognosy*, **2(1)**, 3 (2023) https://doi.org/10.35702/Pharmacogn.10003.

[23] Napit M. Formulation and Evaluation of Herbal Tablets Containing Ethanolic Extract of *Acalypha indica* – A Quality by Design (QbD) Approach. *Research Gate Preprint*, **1(1)**, 1-10 (2024) https://doi.org/10.13140/RG.2.2.15967.82082.

[24] Gupta D, Biswas AA, Sahu RC, Arora S, Agrawal AK. Advancing Pharmaceutical Intelligence via Computational Prognostication of In-Vitro Parameters of Fast Disintegrating Tablets Using Machine Learning Models. *Eur J Pharm Biopharm*, **198(1)**, 112-124 (2024) https://doi.org/10.1016/j.ejpb.2024.09.005.

[25] Rather GJ, Hamiduddin, Ikram M, Naquibuddin M. Formulation and In Vitro Evaluation of Tablet Dosage Form of Unani Anti-Diabetic Powder Containing *Gymnema sylvestre*, *Syzygium cuminii* and *Zingiber officinale*. *Pharmacognosy Research*, **15(3)**, 566-577 (2023) https://doi.org/10.5530/pres.15.3.060.

[26] Dolas RT.Formulation development and evaluation of orodispersible tablet of Azelnidipine by factorial design and its comparison with the marketed formulation. *Particulate Science and Technology*, **41(7),** 1053–1061(2023) https://doi.org/10.1080/02726351.2023.2173109.