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FORMULATION AND EVALUATION OF BUSPIRONE HYDROCHLORIDE BUCCAL TABLETS USING OKRA GUM AS A NATURAL MUCOADHESIVE POLYMER

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Abstract: The present study was aimed at the formulation and evaluation of Buspirone Hydrochloride buccal tablets using Okra gum as a natural mucoadhesive polymer. Buspirone Hydrochloride buccal tablets were prepared by the direct compression method using Okra gum as the natural mucoadhesive polymer. A Quality by Design (QbD)-based Response Surface Methodology (RSM) approach was employed for formulation development and optimization using a randomized Box–Behnken design. The prepared formulations were subjected to preformulation and post-compression evaluation studies.FTIR studies indicated the absence of significant chemical incompatibility between the drug and selected excipients. The powder blends exhibited satisfactory micromeritic properties, with bulk density ranging from 0.419 to 0.438 g/mL, tapped density from 0.512 to 0.552 g/mL, compressibility index from 14.84 to 21.20%, Hausner ratio from 1.17 to 1.27, and angle of repose from 26.0° to 30.5°, indicating suitability for direct compression. The prepared F1–F12 buccal tablets were evaluated for weight variation, thickness, hardness, friability, drug content, disintegration time and swelling index. The tablet weight ranged from 297 to 302 mg, thickness from 3.1 to 3.5 mm, hardness from 3.76 to 4.30 kg/cm², and friability from 0.37 to 0.46%. The drug content ranged from 82.15 to 96.18%, while the disintegration time ranged from 15.8 to 20.1 min. The swelling index of the formulations ranged from 63 to 128%, demonstrating the swelling and hydration ability of Okra gum. In vitro drug release studies were carried out using USP Type II dissolution apparatus in 900 mL of pH 6.8 phosphate buffer at 37 ± 0.5°C for 8 h. All formulations exhibited progressive drug release throughout the study period. Among the formulations, F3 showed the highest cumulative drug release of 97.42% at 8 h, along with a drug content of 96.18% and swelling index of 128%. The observed results indicated that the concentration of Okra gum and other formulation components influenced the swelling and drug-release behavior of the buccal tablets. The selected formulation F3 was subjected to stability studies for 90 days under different storage conditions. The cumulative drug release showed only a gradual change from 97.42% initially to 94.59%, 94.42% and 94.36% after three months under 25°C/60% RH, 30°C/75% RH and 40°C/75% RH conditions, respectively. No appreciable changes were observed during the study period, indicating satisfactory stability of the formulation. The study demonstrated that Okra gum can be used as a natural mucoadhesive polymer in the development of Buspirone Hydrochloride buccal tablets. The developed formulation exhibited satisfactory physicochemical characteristics, swelling behavior and prolonged drug release and may provide a promising approach for buccal delivery of Buspirone Hydrochloride.

Keywords: Buspirone Hydrochloride, Buccal tablets, Okra gum, Natural mucoadhesive polymer, Direct compression, Sustained drug release, Stability study.

INTRODUCTION

Okra gum is a natural polysaccharide obtained from the fruits (pods) of Abelmoschus esculentus belonging to the family Malvaceae. It is a biodegradable, biocompatible, non-toxic, and cost-effective natural polymer widely used in pharmaceutical formulations. The mucilage extracted from okra consists

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mainly of galactose, rhamnose, and galacturonic acid residues, which contribute to its excellent swelling, mucoadhesive, and film-forming properties. Due to its ability to absorb water and form a viscous gel, okra gum has gained considerable attention as a pharmaceutical excipient for controlled-release, sustained-release, and mucoadhesive drug delivery systems. The natural origin, availability, and safety profile of okra gum make it a suitable alternative to synthetic polymers. In buccal drug delivery systems, okra gum acts as a mucoadhesive polymer, enhancing the residence time of the dosage form on the buccal mucosa and improving drug absorption. Its swelling behavior promotes intimate contact between the tablet and mucosal surface, facilitating prolonged drug release and improved bioavailability.

Buccal Drug Delivery System

The unique environment of the oral cavity offers its potential as a site for drug delivery. Because of the rich blood supply and direct access to systemic circulation, the oral mucosal route is suitable for drugs, which are susceptible to acid hydrolysis in the stomach or which are extensively metabolized in the liver (first pass effect) . The total area of the oral cavity is about 100 cm^2. Out of this about one third is the buccal surface, which is lined with an epithelium of about 0.5 mm thickness. The oral mucosal surface is constantly washed by the saliva (daily turn out is about 0.5 to 2 liters) . The continuous secretion of saliva results in rapid removal of released drug. Conversely, the thin mucin film, which exists on the surface of the oral mucosa, may provide an opportunity to retain a drug delivery system in contact with the mucosa for prolonged periods if it is designed to be mucoadhesive. Such systems ensure a close contact with absorbing membrane, thus optimizing the drug concentration gradient across the biological membrane and reducing the differential pathway. Therefore, the buccal (oral) mucosa may be a potential site for controlled or sustained drug delivery. Buccal route of drug delivery is a good alternative, amongst the various routes of drug delivery. Buccal drug delivery is most advantageous because its abundant blood supply in buccal mucosa, bypassing the hepatic first pass effect and accessibility. However, paroral administration of drugs has disadvantages such as hepatic first pass metabolism and enzymatic degradation within the GI tract, that prohibit oral administration of certain classes of drugs especially peptides and proteins. Consequently, other absorptive mucosae are considered as potential sites for drug administration. Oral cavity has been investigated for number of applications including the treatment of periodontal disease bacterial and fungal infection, aphthous and dental stomatitis. Over the last two decades mucoadhesion has become of interest for its systemic delivery by retaining a formulation intimate contact with buccal cavity. The term bio adhesion has been used to define the attachment of a synthetic natural macromolecule to a biological tissue for an extended period of time. When a substrate is a mucosal system adheres and interacts primarily with the mucus layer, this phenomenon being referred to as mucoadhesion. The adhesive properties of such drug delivery platforms can reduce the enzymatic degradation due to the increased intimacy between the delivery vehicle and the absorbing membrane. The use of mucoadhesive polymers in buccal drug delivery has a greater application. Various mucoadhesive devices, including tablets, films, patches, disks, strips, ointments and gels, have recently been developed. However, buccal patch offers greater flexibility and comfort than the other devices. In addition, a patch can circumvent the problem of the relatively short residence time of oral gels on mucosa, since the gels are easily washed away by saliva. Buccal route of drug delivery provides the direct access to the systemic circulation through the jugular vein bypassing the first pass hepatic metabolism leading to high bioavailability.

MATERIALS

Buspirone Hydrochloride was procured from Hetero Labs, Hyd, Okra gum, MCC, Lactose ,Magnesium stearate, Talc and Micro crystalline cellulose were obtained from Synpharma Research Labs, Hyderabad. Other chemicals and the reagents used were of analytical grade.

METHODOLOGY

Extraction of Okra Gum

Fresh okra pods were collected and washed thoroughly with distilled water to remove dirt and other impurities. The pods were cut into small pieces and dispersed in an adequate quantity of distilled water. The dispersion was stirred continuously to facilitate the release of mucilage from the okra pods. The resulting viscous mixture was filtered through muslin

cloth to separate the gum from the plant debris. The collected gum was then dried in a hot air oven at 40–50°C until a constant weight was obtained. The dried mass was pulverized, passed through sieve No. 80 to obtain a fine powder, and stored in an airtight container for further use as a natural mucoadhesive polymer.

Percentage Yield = Weight of dried okra gum obtained \ Weight of fresh okra used *100

Table-1: Formulation of Buspirone Hydrochloride Buccal Tablets Using Box–Behnken Design

	INGREDIENTS (mg)						
S. NO	Buspirone Hydrochloride	Okra gum	MCC	Lactose	Talc	Magnesium Stearate	Saccharine
RUN 1	10	25	10	250.5	2	1.5	1
RUN 2	10	25	10	250.5	2	1.5	1
RUN 3	10	25	10	250.5	2	1.5	1
RUN 4	10	25	10	250.5	2	1.5	1
RUN 5	10	62.5	20	202.25	2	2.25	1
RUN 6	10	62.5	20	202.25	2	2.25	1
RUN 7	10	62.5	20	202.25	2	2.25	1
RUN 8	10	62.5	20	202.25	2	2.25	1
RUN 9	10	100	30	154	2	3	1
RUN 10	10	100	30	154	2	3	1
RUN 11	10	100	30	154	2	3	1
RUN 12	10	100	30	154	2	3	1

Experimental Design and Optimization

A Quality by Design (QbD)-based experimental design approach was employed for the formulation and optimization of Buspirone Hydrochloride buccal tablets. Response Surface Methodology (RSM) was used to investigate the influence of selected formulation variables on the critical quality attributes of the developed buccal tablets. A randomized Box–Behnken design (BBD) was selected as the experimental design. The design was generated using Design-Expert® software. The Box–Behnken design was selected because it allows evaluation of the main effects, interaction effects, and quadratic effects of the selected independent variables with a relatively small number of experimental runs. The experimental design consisted of 12 randomized runs, and a quadratic model was selected for analysis of the responses. The study was conducted with no blocks. The formulation variables were selected based on preliminary formulation trials and their expected influence on the performance of the buccal tablets. The selected independent variables were the concentrations of okra gum and MCC, while the quantities of the remaining excipients were adjusted to maintain a constant total tablet weight of 300 mg. The responses evaluated included drug content, swelling index, and cumulative drug release. The experimental data obtained from each formulation were entered into Design-Expert® software and subjected to statistical analysis. Analysis of variance (ANOVA) was used to determine the significance of the fitted model and the effects of the independent variables on the selected responses. The optimized formulation was selected based on the desirability function, considering the predetermined criteria for the individual responses. The optimized formulation was subsequently prepared and evaluated to verify the predicted response values. Post compression parameters

Post compression parameters

Weight variation:

Twenty tablets were randomly selected form each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weight deviates from the average weight by more than the percentage shown in Table No 1 and none deviate by more than twice the percentage shown.

Thickness

Twenty tablets were randomly selected form each batch and their thickness was measured by using Vernier caliper. Thickness of three tablets from each batch was measured and mean was calculated.

Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm². Three tablets were randomly picked and hardness of the tablets were determined.

Friability:

Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche friabilator was used for the purpose. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at distance of 6 inches with each revolution. Twenty tablets were weighed and placed in the Roche friabilator, which was then operated for 25 rpm for 4 min. After revolution Tablets were dedusted and reweighed.

Compressed tablets should not lose more than 1% of their weight.

Content Uniformity

Twenty tablets from each batch were powdered and weighed accurately equivalent to 100 mg Buspirone Hydrochloride. Dissolve the weighed quantity of powder into 100 ml of 6.8 phosphate buffer solution by stirring it for 15 min. 1 ml of solution was pipette out into 10 ml volumetric flask and make up the volume with distilled water. Immediately analyze the drug by taking absorbance at 237 nm using reagent blank.

Disintegration Test

The disintegration test was performed using a USP disintegration test apparatus. Six tablets were placed individually in the tubes of the basket rack assembly. The apparatus was operated in distilled water maintained at 37 ± 0.5°C. The time required for complete disintegration of each tablet was recorded. The average disintegration time was calculated and reported. For conventional tablets, complete disintegration is expected within the specified pharmacopeial limits. However, for mucoadhesive buccal tablets, a longer disintegration time may be observed due to the presence of mucoadhesive polymers, which are designed to hydrate, swell, and provide prolonged residence at the buccal mucosa.

Swelling index

Swelling index study the extent of swelling was measured in terms of percentage weight gain by the tablet. The swelling index of all formulation was studied. One tablet from each batch was kept in a Petridis containing 2% agar gel plates with the core facing the gel surface and incubated at 37±1 °C. The tablet was removed every two-hour interval up to 12 hour and excess water blotted carefully using filter paper.56 The swollen tablets were re-weighed (Wt). The swelling index (SI) of each tablet was calculated according to the following equation.

$$SI = (W t - W 0)$$

Where

W0 = initial weight,

Wt = weight after time t.

In- Vitro Release study

In-Vitro drug release studies were carried out using Tablet dissolution test apparatus USP II at 50 rpm. The dissolution medium consisted of 900 ml of pH 6.8 maintained temperature at 37±0.5°C.The sample of 1ml was withdrawn at predetermined time intervals and an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced. From that 1 ml sample, 1 ml sample was withdrawn and placed in a 10 ml volumetric flask, and make the volume with buffer. The diluted samples were assayed at 237 nm against reagent blank.

Stability studies

The success of an effective formulation can be evaluated only through stability studies. The purpose of stability testing is to obtain a stable product which assures its safety and efficacy up to the end of shelf life at defined storage conditions and peak profile. The prepared Buspirone Hydrochloride buccal tablets were placed on plastic tubes containing desiccant and stored at ambient conditions, such as at room temperature, 40±2oc and refrigerator 2-8oc for a period of 90 days.

RESULTS AND DISCUSSION

Post compression parameters

Table-4: Evaluation parameters of Buspirone Hydrochloride buccal tablets

F. No.	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm2)	Friability (%)	Drug Content (%)	Disintegration test	Swelling index
F1	298	3.5	4.10	0.45	92.29	18.4	63
F2	301	3.2	3.98	0.46	91.27	16.2	75
F3	300	3.2	4.26	0.41	96.18	20.1	128
F4	299	3.4	3.86	0.42	90.16	15.8	110
F5	299	3.1	3.76	0.43	93.14	17.2	101
F6	301	3.4	3.89	0.38	95.21	19.2	69
F7	298	3.3	3.76	0.43	92.76	16.5	118
F8	297	3.5	4.12	0.37	94.68	18.5	69
F9	301	3.5	4.30	0.39	86.39	17.4	121
F10	299	3.1	4.21	0.44	82.15	17.9	92
F11	302	3.4	4.10	0.43	90.12	16.3	96
F12	299	3.1	3.98	0.39	91.36	15.9	102

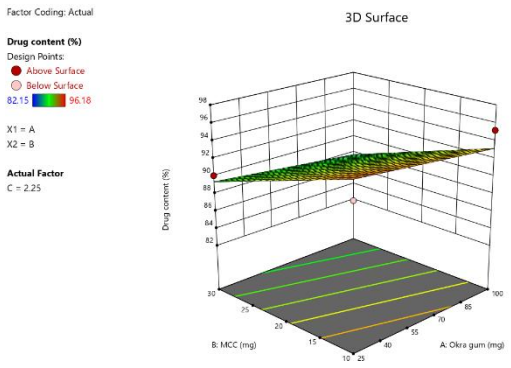


Fig:-1 Response Surface Plot Illustrating Effect of Variables on Drug Content

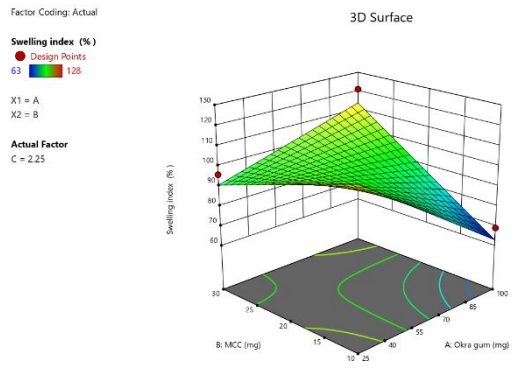


Fig:- 2 Response Surface Plot Illustrating Effect of Variables on Swelling index

Weight Variation:

All the formulated F1 to F12 Buspirone Hydrochloride buccal tablets passed the weight variation test, as the individual tablet weights were found to be within the permissible pharmacopoeial limits. The tablet weights ranged from 297 to 302 mg, indicating good uniformity in tablet weight. The low variation observed among the formulations suggests that the powder blends possessed satisfactory flow and packing characteristics during compression.

Thickness:

The thickness of the formulated F1 to F12 buccal tablets was found to be in the range of 3.1 to 3.5 mm. The relatively small variation in thickness among the formulations indicates uniform die filling and consistent compression during tablet manufacture. The results demonstrate satisfactory dimensional uniformity of the prepared buccal tablets.

Hardness:

The measured hardness of the tablets from F1 to F12 ranged from 3.76 to 4.30 kg/cm². The observed hardness values indicate that the tablets possessed adequate mechanical strength to withstand handling, packaging and transportation without excessive breakage. Formulation F9 showed the highest hardness (4.30 kg/cm²), whereas F7 showed the lowest hardness (3.76 kg/cm²). Overall, all formulations exhibited satisfactory hardness characteristics.

Friability:

The percentage friability of the prepared F1 to F12 formulations ranged from 0.37 to 0.46%. The friability values were below 1% for all formulations, indicating adequate mechanical strength and resistance to abrasion during handling. The results confirm that the compression conditions and excipient combination produced physically stable buccal tablets.

Content Uniformity:

The percentage drug content of Buspirone Hydrochloride in formulations F1 to F12 ranged from 82.15 to 96.18%. Among the formulations, F3 showed the highest drug content of 96.18%, whereas F10 showed the lowest drug content of 82.15%. The variation in drug content may be related to differences in the formulation composition and powder mixing characteristics. Overall, the results indicated satisfactory drug incorporation in most formulations.

Disintegration Time:

The disintegration time of the prepared F1 to F12 buccal tablets ranged from 15.8 to 20.1 min. The disintegration behavior of the tablets is influenced by the nature and concentration of the hydrophilic polymer, diluent and other excipients present in the formulation. The incorporation of Okra gum may influence water uptake, hydration and matrix formation, thereby affecting the disintegration behavior. F4 exhibited the shortest disintegration time (15.8 min), while F3 showed a comparatively higher disintegration time (20.1 min). The observed differences indicate that formulation composition had an influence on the disintegration characteristics of the prepared buccal tablets.

Swelling Index:

The swelling index of the formulated F1 to F12 buccal tablets ranged from 63 to 128%. The variation in swelling behavior may be attributed primarily to differences in the concentration of Okra gum and its ability to absorb the aqueous medium and form a hydrated polymeric matrix. F3 exhibited the highest swelling index of 128%, indicating greater water uptake and swelling capacity. F6 and F8 showed comparatively lower swelling indices of 69%, whereas F1 showed a swelling index of 63%. The higher swelling capacity observed in selected formulations may be advantageous for maintaining the tablet at the buccal site and promoting prolonged drug release.

Dissolution studies

All the 12 formulation of Buspirone Hydrochloride buccal tablets were subjected to in vitro drug release studies these

studies were carried out using dissolution apparatus. The dissolution medium consisted of 900 ml of Standard buffer pH 6.8 for period of time.

Table-5: Drug release studies of all formulations

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
0	0	0	0	0	0	0	0	0	0	0	0	0
1	17.89	16.80	16.62	16.52	19.28	16.98	14.93	19.62	15.12	14.16	13.48	15.28
2	29.86	24.76	28.62	28.91	32.25	29.23	28.82	37.55	25.79	25.91	27.50	26.91
3	35.15	34.90	36.63	35.45	40.87	41.68	37.89	44.78	38.82	37.82	38.93	39.55
4	43.59	45.85	48.82	43.25	52.39	50.36	49.15	50.27	49.18	47.93	45.12	48.26
5	58.12	57.46	62.64	59.88	63.96	61.85	63.25	65.28	62.85	69.15	68.55	67.24
6	69.85	65.83	76.42	70.21	70.83	69.94	71.50	72.85	77.45	72.15	72.11	76.18
7	75.53	74.88	84.54	80.25	83.60	83.86	82.55	84.64	88.93	87.80	86.07	82.14
8	91.28	92.42	97.42	93.65	94.85	92.63	94.32	96.52	95.90	92.66	91.52	93.58

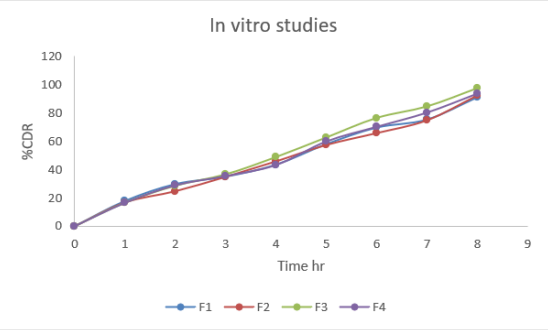


Fig-: 3 Dissolution Profile of F1to F4 formulations

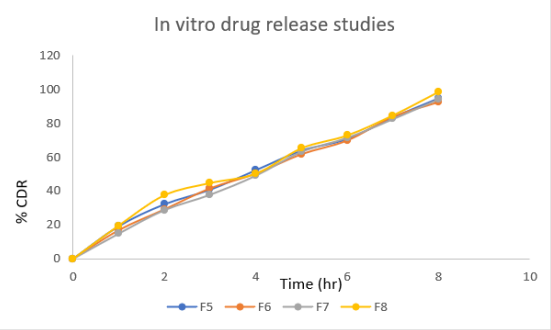


Fig-:4 Drug release studies of (F5-F8) formulations

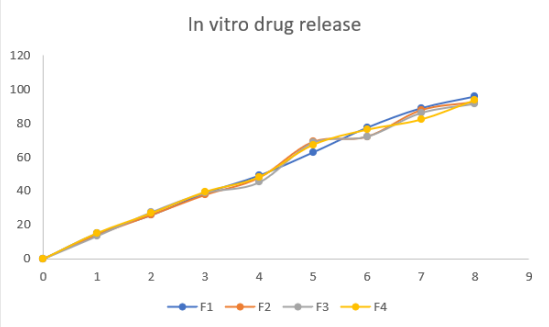


Fig-:5 Drug release studies of (F9-F12) formulations

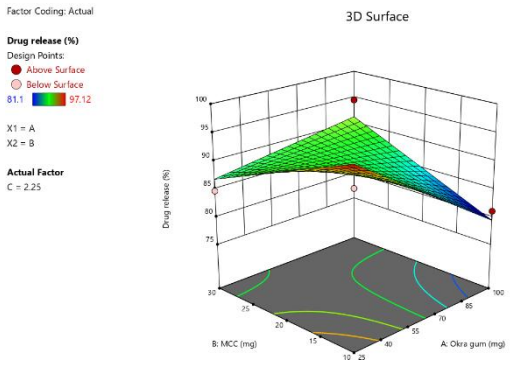


Fig:-6 Response Surface Plot Illustrating Effect of Variables on Drug release

Discussion: The in-vitro drug release studies of all formulations were carried out in pH 6.8 phosphate buffer for 8 hours. All formulations showed gradual and progressive drug release throughout the study period. The cumulative drug release ranged from 91.28% to 97.42%.Among all formulations, F3 showed the highest drug release of 97.42% at 8 hours. The improved release of F3 may be attributed to its satisfactory swelling behavior, which facilitated hydration of the polymer matrix and diffusion of the drug. F3 also showed high drug content and the highest swelling index. Based on the overall drug release results, formulation F3 was selected as the optimized formulation. The results indicate that Okra gum can effectively provide prolonged and controlled drug release from Buspirone Hydrochloride buccal tablets.

Stability Study

There was no significant change in physical and chemical properties of the buccal tablets of formulation F-3 after 90 days. Parameters quantified at various time intervals were shown.

Table-6: Stability studies of all formulations

Formulation Code	Parameters	Initial	1st Month	2nd Month	3rd Month	Limits as per Specifications
F-3	250C/60%RH % Release	97.42	96.69	95.38	94.59	Not less than 85 %
F-3	300C/75% RH % Release	97.42	96.52	95.15	94.42	Not less than 85 %
F-3	400C/75% RH % Release	97.42	96.86	95.05	94.36	Not less than 85 %

Discussion: The optimized formulation F3 was subjected to stability studies for 90 days under different storage conditions. The initial drug release was 97.42%, which gradually decreased

to 94.59%, 94.42% and 94.36% after three months at 25°C/60% RH, 30°C/75% RH and 40°C/75% RH, respectively. Only a slight reduction in drug release was observed during the storage period, and all values remained above the specified limit of not less than 85%. No significant changes in the overall characteristics of the formulation were observed. Therefore, the optimized formulation F3 demonstrated satisfactory stability under the tested storage conditions for the period of 90 days.

SUMMARY AND CONCLUSION

The present study was carried out to formulate and evaluate Buspirone Hydrochloride buccal tablets using Okra gum as a natural mucoadhesive polymer. The buccal tablets were prepared by the direct compression method, and a Quality by Design-based Box–Behnken experimental design approach was employed for formulation development and optimization. The prepared formulations were evaluated for various pre-compression and post-compression parameters. The powder blends exhibited satisfactory micromeritic properties and were found to be suitable for direct compression. The prepared buccal tablets were evaluated for weight variation, thickness, hardness, friability, drug content, disintegration time and swelling index. The weight of the tablets ranged from 297 to 302 mg, indicating satisfactory weight uniformity. The thickness ranged from 3.1 to 3.5 mm, demonstrating acceptable dimensional uniformity. The hardness values ranged from 3.76 to 4.30 kg/cm², indicating adequate mechanical strength. The friability values ranged from 0.37 to 0.46%, which were within acceptable limits. The drug content of the formulations ranged from 82.15 to 96.18%, with formulation F3 showing the highest drug content. The disintegration time ranged from 15.8 to 20.1 minutes. The swelling index ranged from 63 to 128%, demonstrating the hydration and swelling capacity of Okra gum. Formulation F3 exhibited the highest swelling index of 128%. The in-vitro drug release study demonstrated progressive drug release from all formulations over a period of 8 hours. The cumulative drug release ranged from 91.28 to 97.42%. Among all formulations, F3 showed the highest cumulative drug release of 97.42% at 8 hours. Based on the overall evaluation parameters, including drug content, swelling index and in-vitro drug release, F3 was selected as the optimized formulation. The optimized formulation F3 was subjected to stability studies for 90 days under different storage conditions. The formulation showed only a gradual reduction in drug release during storage. After three months, the cumulative drug release was 94.59%, 94.42% and 94.36% at 25°C/60% RH, 30°C/75% RH and 40°C/75% RH, respectively. The drug release remained above the specified limit of not less than 85% under all storage conditions, indicating satisfactory stability of the formulation.

Conclusion

The present study successfully demonstrated the formulation and evaluation of Buspirone Hydrochloride buccal tablets using Okra gum as a natural mucoadhesive polymer. The prepared tablets exhibited satisfactory physicochemical and mechanical properties and were suitable for buccal drug delivery. Okra gum showed good swelling and hydration properties, which contributed to the formation of a hydrated matrix and influenced the drug release behavior of the buccal tablets. Among the prepared formulations, F3 was identified as the optimized formulation based on its satisfactory drug content of 96.18%, maximum swelling index of 128%, and highest cumulative drug release of 97.42% after 8 hours. The stability study of the optimized formulation demonstrated that the formulation maintained satisfactory drug release characteristics under different storage conditions for a period of 90 days. The percentage drug release remained above the specified limit under all tested conditions. Overall, the findings of the present study suggest that Okra gum can be effectively utilized as a natural mucoadhesive polymer for the formulation of Buspirone Hydrochloride buccal tablets. The developed formulation provides sustained drug release and satisfactory stability and represents a promising approach for buccal delivery of Buspirone Hydrochloride. Further studies on mucoadhesive strength, ex-vivo permeation and in-vivo performance may be useful for further evaluation of the developed formulation.

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