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ORIGINAL ARTICLE

Formulation and Evaluation of Fast Dissolving Oral Dosage Forms Containing Dietary Supplements

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ABSTRACT

Background: Dysphagia is a common issue across all age groups, particularly with solid dosage forms. The development of fast-dissolving oral dosage forms has gained significant attention due to their convenience and improved patient compliance. This study focuses on the formulation and evaluation of fast-dissolving oral dosage forms containing dietary supplements, aiming to enhance the bioavailability and efficacy of these supplements.

Methods: Tablets were designed using the direct compression method with an effervescent mixture of sodium bicarbonate, citric acid, and tartaric acid, as well as super disintegrants such as Crospovidone and croscarmellose sodium, both individually and in combination. Veegum-F (magnesium aluminium silicate) was utilised for masking the taste of the vitamins. The prepared tablets were evaluated for hardness, friability, drug content uniformity, wetting time, water absorption ratio, and in vitro dispersion time.

Findings: By incorporating taste-masking agents and an effervescent mixture, the formulation ensures rapid disintegration and improved palatability. Formulation F5, which utilized the effervescent mixture and taste-masking agent, was identified as the optimal formulation based on its in vitro dispersion time (approximately 70-80 seconds), short-term stability (maintained at 40°C/75% RH for 3 months), and drug-excipient interaction results from IR spectroscopy. Stability studies of formulation F5 demonstrated no significant changes in drug content or in vitro dispersion time, confirming its effectiveness and reliability.

Novelty: The potential use of fast-dissolving oral dosage forms in enhancing the delivery of dietary supplements, offers a practical solution for individuals seeking efficient and convenient supplementation.

Keywords: Croscarmellose sodium; Crospovidone; Fast dissolving tablets; Effervescent Mixture; Vitamin B Complex; Vitamin C

INTRODUCTION

Despite of numerous innovations in drug delivery method, the oral route continues to be the preferred route for delivering therapeutic agents due to its accurate dosage, low-cost therapy, self-medication, and ease of self-administration leading to high level of patient compliance. The hard gelatin capsules and conventional tablets are the most commonly used dosage forms. Geriatric and pediatric patients may have difficulties in chewing or swallowing pharmaceuticals that are intended for oral administration[1]. The tablets that dissolve rapidly when in contact with saliva in the buccal cavity, may offer a convenient and effective solution to existing issues and hence there is a growing interest in fast-dissolving tablets for sublingual, buccal, and oral administration for their potential to address various challenges associated with conventional dosage forms[2]. Oral drug administration is a widely accepted method, accounting for 50-60% of all dosage forms, and is considered the most convenient and preferred route for systemic effects due to its ease of dosing administration, pain avoidance, accurate dosage, patient compliance and flexibility in formulation[3,4]. Fast-disintegrating oral dosage forms (capsules or tablets) are a relatively recent dosage technology which allows for the rapid dissolution or disintegration of the dosage form into a suspension or solution in the mouth, without the requirement for water[5]. The disintegration of the dosage form commences as soon as it contacts saliva, with complete breakdown typically accomplished within 30 to 50 seconds following administration[6]. Orally disintegrating tablets, also referred to as Orodispersible tablets (ODTs),

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are tablets that dissolve easily and quickly in the mouth within three minutes before being swallowed. The European Pharmacopoeia uses this term to describe such tablets. The United States FDA (Food and Drug Administration) define orodispersible tablet as "a solid dosage form comprising an active ingredient or medicinal substance that rapidly disintegrates, typically in a matter of seconds, when placed on the tongue." The time it takes for orodispersible tablets to disintegrate typically falls between a few seconds and approximately one minute[7]. As the demand for patient-compliant dosage forms increases, pharmaceutical companies are prioritizing improvements in drug delivery systems. B vitamins- Thiamine (B1), Riboflavin (B2), Niacin (B3), Pantothenic Acid (B5), Pyridoxine (B6), Folic Acid (B9), and Vitamin B12- are crucial water-soluble nutrients necessary for metabolism, immune function, and cell growth. Daily replenishment of these vitamins is essential to prevent deficiencies, which can lead to significant health issues. The objective of this study is to overcome the challenges of dysphagia, particularly among the elderly, pediatric populations, and others affected by swallowing difficulties, by developing fast-dissolving tablets that dissolve in saliva without the requirement of water, facilitating easier drug absorption.

METHODOLOGY

Instruments used

Precise measurements were taken with the use of a Sartorius weighing balance, while moisture content was analyzed with a Sartorius moisture analyzer. Humidity levels were monitored with an Equimox hygrometer and tablet compression was performed using two machines: the Rimek Minipress (12 Station) and the Cadmach (16 Station). Disintegration testing was carried out with an Electrolab USP disintegration tester, and friability was assessed using an Electrolab USP friabilator. Bulk and tap densities were measured with an Electrolab USP apparatus. Stability studies were conducted in a Newtronics stability walk-in chamber. Infrared spectroscopy was performed with a Jasco FTIR, and HPLC (high-performance liquid chromatography) analysis was conducted using an Agilent HPLC system.

Preformulation studies

Drug Profile

The physicochemical properties of the vitamins were evaluated, including their description, crystallinity, odor, solubility, identification by infrared spectroscopy (IR), loss on drying, melting point, heavy metals content, and assay.

Active pharmaceutical ingredients (API

The formulation used APIs from Strides Arcolab: Calcium Pantothenate, Folic Acid, Nicotinamide, Thiamine Hydrochloride, Riboflavin, Pyridoxine Hydrochloride, Cyanocobalamin, and Ascorbic Acid.

Selection of excipients

Excipients were chosen to enhance disintegration and ensure compatibility with vitamins, including diluents, effervescent mixture, super disintegrants, taste masking agents, sweeteners, flavourings, lubricants, and glidants.

Excipients used

The formulation included several excipients, each with a specific role: Isomalt (Galen IQ) as a diluent, Veegum-F (Magnesium Aluminium Silicate) (Pioma Chemicals) as a taste-masking agent, Tartaric Acid, Sodium Bicarbonate, and Citric Acid (Strides Acrolab) for the effervescent mixture, Crospovidone and Croscarmellose Sodium (Strides Acrolab) as super disintegrants, Orange Flavour (Givovidan & Sonorome) and Menthol (Strides Acrolab) for flavouring and taste bud desensitization, Sucralose and Liquorice (Strides Acrolab) as sweeteners and Magnesium Stearate and Talc (Strides Acrolab) as a lubricant and glidant, respectively.

Drug-excipient compatibility studies by Infra-red spectroscopy

Infra-red spectroscopy was used to identify functional groups in the drug and excipients to confirm their chemical identity and compatibility.

Formulation of fast dissolving tablets of vitamin 'B' complex and vitamin 'C'

Water-soluble B vitamins were chosen as ideal candidates for fast-dissolving tablets for formulation. The selected vitamins include Calcium Pantothenate (B5), Folic Acid (B9), Niacinamide (B3), Thiamine Hydrochloride (B1), Riboflavin (B2), Pyridoxine Hydrochloride (B6), Cyanocobalamin (B12), and Ascorbic Acid (C). Fast-dissolving tablets of the Vitamin B Complex were prepared using the method of direct compression.

Formulation with super disintegrants

All ingredients, except the super disintegrant, magnesium stearate, and talc, were sieved through a #40 mesh. The APIs, Veegum-F, and isomalt were mixed in small portions to achieve uniformity. Super disintegrant, magnesium stearate, and talc were sieved through a #60 mesh. Both mixtures were blended in an octagonal blender for 15-20 minutes, then compressed using a hydraulic press. The compression force was adjusted to achieve tablet hardness of 30-40 Newtons, with tablet weight kept constant at 550 mg for formulations F1 to F3.

Formulation with effervescent mixture

Effervescent tablet preparation required maintaining at 20-30% RH and temperatures below 30°C. Ingredients,

except for the effervescent mixture, magnesium stearate, and talc, were sieved through a #40 mesh. APIs, Veegum-F, and isomalt were blended in small portions to achieve uniformity. The effervescent mixture, magnesium stearate, and talc were sieved through a #60 mesh. Both mixtures were then blended in an octagonal blender for 15-20 minutes before immediate compression. Tablets were compressed with a hydraulic press to achieve a hardness of 30-40 Newtons, with a constant weight of 550 mg for formulations F4 to F7 (Table 1).

Table 1: Composition of different batches of fast dissolving tablets of vitamin 'B' complex and vitamin 'C'

Ingredients (mg/tab)	Formulation Code						
	F1	F2	F3	F4	F5	F6	F7
Thiamine Hydrochloride (B_1)	2.1	2.1	2.1	2.1	2.1	2.1	2.1
Riboflavin (B_2)	1.95	1.95	1.95	1.95	1.95	1.95	1.95
Niacinamide (B_3)	24	24	24	24	24	24	24
Calcium Pantothenate (B_5)	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Pyridoxine Hydrochloride (B_6)	1.95	1.95	1.95	1.95	1.95	1.95	1.95
Folic Acid (B_9)	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Cyanocobalamine (B12)	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Ascorbic Acid (Vit C)	78	78	78	78	78	78	78
Crospovidone	10	—	10	—	—	—	—
		-		-	-	-	-
Croscarmellose Sodium	—	10	10	—	—	—	—
	-			-	-	-	-
Tartaric Acid	—	—	—	10	30	40	30
	-	-	-				
Citric acid	—	—	—	2	5	10	5
	-	-	-				
Sodium Bicarbonate	—	—	—	10	60	80	60
	-	-	-				
Orange Flavour	10	10	10	10	10	10	10
Menthol	1	1	1	1	1	1	1
Sucralose	25	25	25	25	25	25	25
Liqorice	10	10	10	10	10	10	10
Isomalt	256.2	256.2	246.2	244.2	171.2	136.2	287.6
Veegum-F	116.4	116.4	116.4	116.4	116.4	116.4	—
							-
Talc	3	3	3	3	3	3	3
Magnesium Stearate	2	2	2	2	2	2	2
Total	550	550	550	550	550	550	550

Evaluation of fast dissolving tablets

The purpose of the evaluation was to analyse the physicochemical properties and other characteristics of the developed formulations.

Precompression Parameters

Effervescent components are highly hygroscopic, so precompression parameters were maintained below 40% RH to prevent moisture absorption.

Bulk Density (Db). Bulk density is the ratio of the powder's mass to its bulk volume. It is measured by pouring weighed, sieved powder into a measuring cylinder and noting the initial volume, which is used in the calculation and expressed in g/cc.

Tapped density (Dt). Tapped density is the mass-to-tapped volume ratio of powder. Fifty grams of blend were placed in a 250 ml flask, and the volume was measured after 100 taps expressed in g/cc.

Angle of Repose. The angle of repose is the maximum angle between a powder pile's surface and the horizontal. Powders were allowed to flow through a funnel and form a heap. The angle was calculated from the heap's height and radius. An angle <25° indicates excellent flow, 25-30° good flow, 30-40° passable, and >40° poor flow.

Compressibility Index. Powder flowability is assessed by comparing bulk density (Db) and tapped density (Dt) to calculate the compressibility index. Compressibility ranges indicate flow properties: 5-15% for excellent, 12-16% for good, 18-21% for fair, 23-25% for poor, 33-38% for very poor, and >40% for extremely poor flow.

Hausner's Ratio. The ratio of tapped density to the bulk density was calculated by Hausner's ratio.

Post-compression parameters

Shape of Tablets. Directly compressed tablets were examined under the magnifying lens for the shape of the tablet.

Tablet Dimensions. The measurements for the thickness and diameter were taken using calibrated digital vernier callipers, with 3 tablets from each formulation being randomly chosen and individually measured.

Hardness. Hardness, indicating a tablet's ability to withstand mechanical shocks, was measured in Newtons using a digital hardness tester. A random selection of three tablets was done for testing.

Friability test. friability was measured using a Roche Friabilator. Ten tablets were weighed (WI), placed in the friabilator, and rotated at 25 rpm for 4 minutes or 100 revolutions. The tablets were weighed again (WF) and %

friability wascalculated. A friability <1% was considered acceptable.

Weight Variation Test. Ten tablets from each batch were weighed individually to check weight variation, allowing minor deviations as per U.S. Pharmacopoeia standards.

Test for Content Uniformity. Content uniformity was conducted using HPLC method.

Wetting Time. For formulations with super disintegrants, a Petri dish (5.5 cm diameter) with 6 ml methylene blue dye was used. A tablet placed in the center was observed, and the time to wet the tablet's surface was recorded as wetting time.

In vitro Dispersion Time. A tablet was placed in 10 ml of water at 37±0.5°C, and the time for complete dispersion was measured.

Moisture uptake studies. The study was conducted at 40%, 60%, and 75% RH at 25°C. Five clean Petri dishes were weighed (W1). Ten tablets per dish were weighed (W2). Dishes were placed in a desiccator with a saturated salt solution for each RH and sealed. Initial time was recorded as '0', and weights were measured at 2, 4, 6, 8, 24, 32, and 48 hours. The solubility and relative humidity of Potassium Carbonate was 1.15 g/ml at 40% RH, Sodium Bromide was 1.16 g/ml at 60% RH and Sodium Chloride was 0.37 g/ml at 75% RH.

Assay

The HPLC system, an Agilent equipped with a Photo Diode Array detector, used an Inertial ODS-3V column (250 × 4.6 mm, 5 μm). The column oven was set to 25°C, with a flow rate of 1 mL/min. The analysis was performed at wavelengths of 210 and 268 nm, with an injection volume of 5 μL and a run time of 25 minutes. The mobile phase for the HPLC analysis consisted of two components: Mobile Phase A was a potassium dihydrogen phosphate buffer (pH 2.5), and Mobile Phase B was 100% HPLC-grade methanol.

Standard Preparation:

Standard Preparation 1. Dissolved 20.7 mg Vitamin B2 and 30.24 mg Vitamin B6 in a 20 ml volumetric flask and filled to volume with water.

Standard Preparation 2. Dissolved 6.533 mg Vitamin B1 and 81.02 mg sodium bicarbonate in a 10 ml volumetric flask and filled to volume with water.

Standard 3. Combined 7.501 mg of Vitamin B1, 40.35 mg of Vitamin B3, 15.78 mg of Vitamin B5, 200.5 mg ascorbic acid, 5 ml of Preparation 1, and 1 ml of Preparation 2 in a 50 ml volumetric flask, shook, and filled to volume with water.

Standard Preparation 4. Dissolved 5 mg Vitamin B11 in a 50 ml volumetric flask with 25 ml water and 3-4 sodium carbonate crystals, stirred until dissolved, and filled to volume with water.

Sample Preparation

Weighed 20 Vitamin 'B' Complex tablets and recorded their weight. Triturated the tablets in a clean mortar. Weighed 550 mg of the powder blend, transferred it into a 100 ml amber volumetric flask, and mixed with water. Adjusted the volume with water. Equilibrated the chromatographic system with a gradient program by injecting the blank solution, followed by 10 μl of the standard preparation four times. Ensured that the % RSD for each component was within 5%. Injected 10 μl of the sample preparation, identified each peak by comparing retention times with the standard, and calculated the amount of each ingredient.

Stability Study

The International Conference on Harmonization (ICH) Guidelines on "Stability Testing of New Drug Substances and Products" (QIA) outline stability test requirements for drug registration in the EU, Japan, and the USA. The International Conference on Harmonization guidelines specify that long-term testing is at 25°C ± 2°C with 60% RH ± 5% for 12 months, and accelerated testing is at 40°C ± 2°C with 75% RH ± 5% for 6 months. In this study, stability testing was conducted at 40°C and 75% RH for 2 months. The formulation was packed in moisture-proof containers with silica gel to prevent moisture uptake and stored at 25°C ± 2°C / 60% RH ± 5% for 12 months and 40°C / 75% RH for 6 months. Only the first 2 months of stability results at 25°C ± 2°C / 60% RH and 40°C / 75% RH were reported.

RESULTS AND DISCUSSION

Physicochemical properties of Active ingredients

The Samples of Vitamin 'B' Complex along with Ascorbic acid were tested for physiochemical properties which complied for in house specifications (Table 2).

Formulation of Fast dissolving Vitamin 'B' Complex Tablet

The present study aimed to develop taste-masked formulations of fast-dissolving Vitamin tablets. Vitamin dosages were determined on the basis of "Recommended Dietary Allowance" (RDA), which establishes the nutritional levels needed to meet the requirements of nearly all healthy individuals[8] (Table 2).

Table 2: Drug profile

Sr. No	Tests	Limits / Specifications	Results
Monograph Analysis of Calcium Pantothenate			
1	Description	White or practically white	White
2	Form	Crystalline powder	Crystalline powder
3	Odour	Characteristic odour	
4	Solubility	Freely soluble in water; soluble in glycerin; slightly soluble in ethanol (95%); practically insoluble in ether.	Complies
5	Identification by IR	The infrared absorption spectrum of the sample must be concordant with the standard spectrum	
6	Loss on drying	Not more than 3.0%, determined on 1 g by drying in an oven at 105°	1.2 %
7	Heavy metals	Not more than 20 ppm, on 1.0 g dissolved in 25 ml of water	5 ppm
8	Residue on ignition	Not more than 0.15 %	0.060 %
9	Assay	97.0 - to 103 %	100 %
Monograph Analysis of Folic Acid			
1	Description	Yellow to yellowish-orange	Yellow
2	Form	Crystalline powder	Crystalline powder
3	Odour	Characteristic odour	
4	Solubility	Practically insoluble in cold water and in most organic solvents; very slightly soluble in boiling water; soluble in dilute acids and in alkaline solutions	Complies
5	Identification by IR	The infrared absorption spectrum of the sample must be concordant with the standard spectrum	
6	Sulphated ash	Not more than 0.5%	0.00
7	Assay	99-102 %	100%
Monograph Analysis of Nicotinamide			
1	Description	Colourless crystals or white	White powder
2	Form	Crystalline powder	Crystalline powder
3	Odour	Faint and characteristic	
4	Solubility	Freely soluble in water and in ethanol (95%); slightly soluble in chloroform and in ether.	Complies
5	Identification by IR	The infrared absorption spectrum of the sample must be concordant with the standard spectrum	
6	Heavy metals	Not more than 30 ppm,	5 ppm
7	Melting point	Melts between 128° and 131°	Complies
8	Assay	97.5-102 %	99.5 %
Monograph Analysis of Thiamine Hydrochloride			
1	Description	Colourless crystals or white	White powder
2	Form	Crystalline powder	Crystalline powder
3	Odour	Characteristic	
4	Solubility	Freely soluble in water and in ethanol (95%); slightly soluble in chloroform and in ether.	Complies
5	Identification by IR	The infrared absorption spectrum of the sample must be concordant with the standard spectrum	
6	Heavy metals	Not more than 20 ppm,	10 ppm
7	Loss on Drying	Not more than 5.0%, determined on 1 g by drying in an oven at 105°	1.5%
8	Assay	98.5 to 101.0%	99.5 %
Monograph Analysis of Riboflavin			
1	Description	Powder	Powder
2	Colour	Orange yellow	Complies

Continued on next page

Table 2 continued

3	Solubility	Very slightly soluble in water; more soluble in saline solution than in water; practically insoluble in chloroform, in ethanol (95%) and in ether.	
4	Specific rotation	-135 to -115^0	-127
5	Loss on drying	Max 1.5%	0.7
6	Sulphated ash	Max0.10%	0.02
7	Heavy metals	10 ppm	complies
8	Lead	<=2 ppm	
Monograph Analysis of Pyridoxine Hydrochloride			
1	Description	White or practically white	White
2	Form	Crystalline powder, pallets or rods	Crystalline powder
3	Odour	Acidic, with slightly bitter saline taste almost odourless	Complies
4	Solubility	Freely soluble in water and in ethanol (95%); slightly soluble in chloroform and in ether.	
5	IR	Complies	
6	Residue on ignition	Not more than 0.15 %	0.060 %
7	Assay	97.0- to 103 %	100 %
Monograph Analysis of Cyanocobalamine			
1	Description	Crystalline powder or Small crystals	Crystalline powder
2	Coloration of aqueous solution (0.050g + 25 ml)	Red	Red
3	Loss on Drying	<= 3.0 %	1.5 %
4	Solubility	Sparingly soluble in water and in ethanol (95%); practically insoluble in chloroform, in acetone and in ether.	Complies
5	Related substances (HPLC)	<=3.0 %	0.9 %
6	Assay by spectroscopy	97.0 to 100.5 %	99.8 %
Monograph Analysis of Ascorbic Acid			
1	Appearance	Powder	Powder
2	Colour	White	White
3	Loss on Drying	0 to 0.1 %	0.01 %
4	Heavy metals	0-10 ppm	<10 ppm
5	Iron	0-2 ppm	1.22 ppm
6	Copper	0-5 ppm	2.546 ppm
7	Lead	0-2 ppm	0.394 ppm
8	Arsenic	0-3 ppm	1.754 ppm
9	Mercury	0-1 ppm	0.698 ppm
10	Oxalic Acid	0-0.2 ppm	0.146 ppm
	Assay		
11	Through USP 20 (850u)	100 to100 %	100 %
12	Through USP 100 (150u)	0 to 70 %	22 %

Compatibility data for the drug and excipients

Sr. No.	Combination/Formulation	Results
1.	Vitamin B Complex + 10mg Crospovidone [F1]	
2.	Vitamin B Complex + 10mg Croscarmellose Sodium [F2]	
3.	Vitamin B Complex + 10mg Crospovidone +10mg Croscarmellose Sodium [F3]	
4.	Vitamin B Complex + 10 mg Tartaric Acid + 2 mg Citric acid + 10mg Sodium Bicarbonate [F4]	Complies
5.	Vitamin B Complex + 30 mg Tartaric Acid + 5 mg Citric acid + 60mg Sodium Bicarbonate [F5]	
6.	Vitamin B Complex + 40 mg Tartaric Acid + 10 mg Citric acid + 80mg Sodium Bicarbonate [F6]	
7.	Vitamin B Complex + 30 mg Tartaric Acid + 5 mg Citric acid + 60 mg Sodium Bicarbonate [F7]	

Representation of RDA Quantity of Vitamins

The recommended daily intake of vitamins varies by age and physiological condition. For adults aged 31-50 years, it is: Calcium Pantothenate 5 mg, Folic Acid 0.4 mg, Nicotinamide 16 mg, Thiamine Hydrochloride 1.2 mg, Riboflavin 1.3 mg, Pyridoxine Hydrochloride 1.3 mg, Cyanocobalamin 0.2 mg, and Ascorbic Acid 60 mg. For children aged 4-8 years: Calcium Pantothenate 3 mg, Folic Acid 0.2 mg, Nicotinamide 8 mg, Thiamine Hydrochloride 0.6 mg, Riboflavin 0.6 mg, Pyridoxine Hydrochloride 0.6 mg, Cyanocobalamin 0.08 mg, and Ascorbic Acid 37 mg. Pregnant and lactating women require: Calcium Pantothenate 6-7 mg, Folic Acid 0.5-0.6 mg, Nicotinamide 17-18 mg, Thiamine Hydrochloride 1.4 mg, Riboflavin 1.4-1.6 mg, Pyridoxine Hydrochloride 1.9-2 mg, Cyanocobalamin 0.8-1 mg, and Ascorbic Acid 87 mg daily. Due to the sensitivity of vitamins to light and environmental conditions, excess quantities, or "overages," are added to ensure sufficient levels[9].

Overages of vitamin in combination products

After finalizing the vitamin doses, various trials were performed using both super disintegrants and effervescent mixtures. Although formulations were prepared, a bitter taste from the vitamins was a problem. To mask the taste, Magnesium Aluminium Silicate (VEEGUM-F) was used. VEEGUM-F, a directly compressible grade, was chosen as the taste-masking agent. Its concentration was optimized by trial and error, with a final ratio of 1:1, meaning an equal proportion of vitamins and VEEGUM-F. Seven formulations were prepared: the first three used combinations of two super disintegrants or single super disintegrants; the next three used different concentrations of effervescent mixtures; and the final formulation used the effervescent concentration from the seventh formulation without the taste-masking agent.

Process involved in optimizing the formulation

The dosage form development involved trials with varying excipient percentages to optimize the formula. Due to the high dose of active ingredients, the goal was to minimize excipients to reduce tablet size for patient compliance and cost-effectiveness. Formulation F-1 used Crospovidone alone as a super disintegrant but had a disintegration time (Dt) of 165 seconds and a bitter taste. The next formulation used Croscarmellose Sodium but still had a DT of 140 seconds and bitterness. The third approach combined Crospovidone and Croscarmellose Sodium, reducing Dt to 103 seconds but increasing bitterness. The fourth approach used a 1:1 ratio of tartaric acid and sodium bicarbonate, reducing Dt to 95 seconds. In the fifth approach, a 1:2 ratio of tartaric acid and sodium bicarbonate further decreased DT to 80 seconds with improved taste and mouthfeel, effectively masking the bitterness. The sixth approach, with a 1:2 ratio of tartaric acid and sodium bicarbonate, reduced Dt to 45 seconds but resulted in an unacceptably tart taste. The seventh approach used the effervescent concentration from F-5 but removed VEEGUM-F, resulting in an undesirable taste. Finally, F-5, which had acceptable assay results, was selected as the optimized formulation and subjected to stability studies (**Supplementary table 1**).

Stability Studies for Optimized formulation

The stability studies followed ICH guidelines. Long-term testing was conducted at 25°C ± 2°C with 60% RH ± 5% for 12 months, and accelerated testing at 40°C ± 2°C with 75% RH ± 5% for 6 months. Reports from the first two months were within acceptable limits, prompting continuation of the study for the next six months (**Supplementary table 1**).

CONCLUSION

The research aimed to create a novel injectable dosage form of betamethasone acetate, which is insoluble in water. The project aimed to overcome its drawbacks and create a stable formulation as a depot injectable suspension. Surfactants like polysorbate 80 and PEG 3350 were selected to improve syringibility, resuspendibility, and sedimentation characteristics. Monobasic and dibasic sodium phosphate were used as buffers, disodium edeate as a complexing agent, and benzalkonium chloride as a preservative. The batch-II formulation was chosen due to its good appearance, syringibility, resuspendibility, drainage, zeta potential, assay, pH, and related impurities. The drug release from the suspension was prolonged for 24 hours. Stability studies were conducted for three months, revealing the formulation's stability.

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