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Formulation development and evaluation of sucrose-free lozenges of curcumin

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Abstract

The Sucrose-free compressed lozenges each containing 300 mgs of Curcumin (Turmeric) were formulated and prepared by standard preparation method using mannitol base and different excipients. The optimized formulation presented as alternative to marketed Ginger throat lozenges to be used in common conditions of cough and cold with vide acceptability among diabetics. The prepared lozenges were evaluated as per I.P. procedures.

1. INTRODUCTION

Curcumin (Turmeric) is commonly used as spice and condiment in many Indian foods. The traditional use of turmeric as an antiseptic is age old in India. The rhizomes are found useful in skin diseases, cough, fever and common cold.[1]

Lozenges are intended to be allowed to dissolve on the rear surface of the mouth to provide drug delivery locally to minimise systemic and maximise local drug activity [2]. Upon chewing/ sucking, they dissolve slowly in the mouth and release their ingredients for local action.[3]

Several candy lozenges intended for sore throat and cough are available in the market but have high content of sucrose as base. Patients suffering from Diabetes mellitus avoid sucrose containing lozenges; hence, it was felt to develop sucrose-free compressed lozenges of Curcumin using mannitol as substitute for sucrose- free base. Mannitol reportedly being metabolically inert in humans and could be used as sugar substitute and may have vide acceptability among diabetics.[4, 20]

Hence in the current study, the mannitol-based compressed lozenges, each containing 300 mgs of Curcumin were formulated and evaluated to be used in common cough and cold as alternative to marketed Ginger candy lozenges.

2. MATERIALS AND METHODS

2.1 Materials

Curcumin powder complying with I.P. 2010 specifications as per its Appendix 13.2, A-159 was procured from Molychem laboratories. All excipients used in the formulation complied with I.P. 2010 specifications. Microcrystalline cellulose (MCC) and polyvinyl pyrrolidone (PVP K-30) were obtained from Dr. Reddy's Laboratories, Hyderabad as gift samples. Mannitol, Aspartame and Citric acid were purchased from SD Fine chemicals, Mumbai. Menthol and purified talc powder were purchased from Molychem Laboratories. Isopropyl alcohol was purchased from E. Merck. Peppermint oil, Camphor, Thymol, Methyl salicylate, Magnesium stearate and Aerosil were procured from Alpha chemical laboratories. The chemicals and reagents used in the study were of Analytical Reagent grade.

2.2 Pre-formulation Studies

2.2.1 Identification of Curcumin powder and other excipients used in the formulations

Curcumin powder was identified by organoleptic evaluation as per specifications laid down in the I.P. 2010. All other excipients were subjected to tests for identity and purity as prescribed in respective monographs given in I.P. 2010 for each sample before using them in the formulations. Since intended formulations were supposed to be sucrose-free; hence, all raw materials used were tested for freedom from traces of sucrose using qualitative and quantitative tests[5] for presence of sucrose. The raw materials which conformed to 'absence of sucrose' were used in the formulations.

2.2.2 Drug-Excipient compatibility Studies

The compatibility studies provide the basis for the selection of excipients for the particular drug in the fabrication of the dosage form. The study was carried out to establish that the therapeutically active drug did not undergo any changes after it was subjected to processing steps along with excipients during formulation of lozenges. The drug and excipients were checked for their compatibility by Fourier Transform Infrared Spectroscopy. The I.R. spectral peaks of pure drug and drug excipients in potassium bromide (KBr) pellets were evaluated using FTIR Spectrophotometer (Bruker series). The compatibility was evidenced from characteristic peaks of individual components and formulation process was Commenced.[6] The drug and excipients compatibility studies were performed by preparing physical mixture of drug and excipients in different ratios (1:1, 1:1, 1:5, 1:10, 1:10) subjecting samples at 50°C for three weeks. At the end of three weeks, the characteristic changes if any were recorded and FTIR spectra of all the samples were taken.

2.2.3 Testing of Raw Materials for absence of Pathogenic microorganisms (Salmonella typhii, Pseudomonas aeruginosa, Staphylococcus aureus, Escherichia coli, Yeast and Mold) as per I.P. 2010 procedures

All raw materials used in preparation of optimized formulation B8 of Curcumin lozenges were tested for absence of pathogenic microorganisms. The Samples were streaked on respective plate medium and checked for growth of specific microorganisms as per **I.P. 2010 procedures**. The inoculated plates were incubated at 37^{0}C for bacteria and at 25-30^{0}C for Yeast and Mold.

2.2.4 Formulation Development

The lozenges, each containing 300 mgs of Curcumin powder were prepared using wet granulation method. The powders used in the formulation were passed through 60 #. Exactly weighed amounts of Menthol Crystals, Peppermint Oil, Camphor and Thymol were mixed together to get a eutectic mixture which was added to measured quantity of methyl salicylate and isopropyl alcohol containing weighed quantity of polyvinyl pyrrolidone (PVP-K30) and mixed well. The resultant liquid mixture (A) was used for granulation. The curcumin powder, mannitol, micro crystalline cellulose, aspartame and citric acid were weighed and sieved through sieve no 80# and were thoroughly mixed to form dry mixture. The liquid mixture (A) above was added to the dry mixture to get dough. The dough thus obtained was sieved through sieve no 12. Wet granules thus obtained were dried in hot air oven at 50^{0}C for 1 hour. Dried granules were passed through sieve no. 20 and retained on sieve no. 40. Magnesium stearate, purified talc and aerosil were weighed and mixed properly and added extra granularly in the above sieved granules. The final blend of granules was mixed thoroughly for 2-3 minutes in polybag and evaluated for various pre-compression parameters described below under 2.3.

The dried granules obtained were compressed on a rotary tablet machine (Cadmach, Ahmedabad) using 15 mm standard flat punches. The compression force was adjusted to yield lozenges with hardness of 4 kg/cm^2 with compression batch of 100 lozenges. The average weight was controlled to 722 mg ± 5 % measured every 15 minutes during compression. The composition of the preliminary trial batches taken for the development of lozenges of Curcumin is described in table 1. Amongst 8 batches prepared, batch no B8 showed good results and acceptability hence B8 was selected as an optimized formulation.

2.3 Pre-compression Evaluation

The flow properties of blend (before compression) were characterized in terms of angle of repose, Bulk density, Tapped density, Carr's index (compressibility index) and Hausner ratio [7].

2.4 Post Compression Evaluation of Curcumin lozenges

2.4.1 Physical Characteristics of compressed Curcumin Lozenges

General appearance, diameter and thickness were noted. [8] The appearance of all lozenges, its visual identity and overall elegance is essential for consumer acceptance. The formulated compressed lozenges were evaluated for size, shape, organoleptic characters such as colour, odour and taste. The diameter and thickness of the lozenges were measured using Micrometre. Twenty lozenges were taken from batch and average thickness and diameter was recorded.

2.4.2 Weight variation / uniformity of weight

Twenty lozenges of each formulation were selected at random and weighed individually and collectively on a digital weighing balance. The weight of individual lozenge was noted. Average weight was calculated and the individual weights were compared with the average weight. The weight of not more than two lozenges must not deviate from the average weight by more than 5 %[9].

Table 1: Composition of preliminary batches of curcumin lozenges

sr. no.	Ingredients	Purpose	Quantity in mgs							
			Batch numbers							
			B1	B2	B3	B4	B5	B6	B7	B8
i	Curcumin powder	Active ingredient	300	300	300	300	300	300	300	300
ii	D-Mannitol	Base	-	-	-	175	175	370	360	350
iii	Dibasic calcium phosphate	Base	374	363	353	178	168	-	-	-
iv	PVP (Polyvinyl Pyrrolidone) K-30	Binder	11	11	11	11	11	11	11	11
v	Microcrystalline cellulose	Diluent	-	10	20	10	20	-	10	20
vi	Aspartame	Sweetening agent	-	-	-	20	20	20	20	20
vii	Citric Acid	Pharmaceutical aid	1	1	1	1	1	1	1	1
viii	Menthol Crystals	Pharmaceutical aid (cooling effect)	1	1	1	1	1	1	1	1
ix	Peppermint oil	Carminative and Pharmaceutical aid	-	-	-	-	-	0.002ml	0.002ml	0.002 ml
x	Camphor	Pharmaceutical aid	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
xi	Thymol	Pharmaceutical aid	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
xii	Methyl salicylate	Fragrant agent	-	-	-	-	-	0.1 ml	0.1 ml	0.1 ml
xiii	IPA (Isopropyl alcohol)	Vehicle	0.4 ml	0.4 ml	0.4 ml	0.4 ml	0.4 ml	0.4 ml	0.4 ml	0.4 ml
xiv	Magnesium stearate	Lubricant	10	10	10	10	10	10	10	10
xv	Purified Talc	Lubricant	-	-	-	-	-	5	5	5
xvi	Aerosil	Free flowing agent	-	-	-	-	-	4	4	4
xvii	Strawberry flavor powder	Flavoring agent	15	15	15	15	15	-	-	-
xviii	Saccharin powder	Sweetening agent	10	10	10	-	-	-	-	-

 # Aspartame: Artificial, non-saccharide sweetener, about 200 times sweeter than sucrose, Saccharin: 300 -400 times sweeter than sucrose.

2.4.3 Hardness

Hardness was measured using Monsanto Hardness tester by taking six lozenges from each formulation. The values were expressed in Kg / cm^2.[9]

2.4.4 Friability

The friability of sample of twenty lozenges were measured using a Roche Fribilator. Twenty pre-weighed lozenges were rotated at 25 rpm for 4 minutes. The lozenges were taken out and de-dusted and were reweighed and the percentage of weight loss was calculated. Friability was found to be less than 1% in the range of 0.15% to 0.99%.[10]

Percentage friability = [(Initial Weight – Final Weight) /Initial Weight] x 100

2.4.5 Wetting Time and water absorption ratio

A piece of tissue paper folded twice was kept in a Petri dish (internal diameter 5.5 cm) containing 6 ml of purified water. A lozenge having a small amount of Rosaline dye powder on the upper surface was placed on the tissue paper. The time required to develop a red colour on the upper surface of the lozenge was recorded as the wetting time.[9,11] The same procedure without Rosaline dye powder was followed for determining the water absorption ratio R which was determined according to the following equation.

$$R = [(W_a – W_b)/W_b] \times 100$$

Where, W_b and W_a were the weights of the lozenges before and after use.

2.4.6 Disintegration Time

Disintegration time was measured in artificial saliva (pH 5.8) according to the USP 24 method at 37 ± 0.5^{0}C. The disintegration time of 6 individual lozenges were recorded[12].

2.4.7 Drug Content and content uniformity

Drug content in all formulations was estimated by U.V. Spectrophotometric method. The content uniformity was determined in each of twenty lozenges Spectrophotometrically.[13]

2.4.8 Moisture Content / Water Content

Moisture content / Water content were determined by using Karl Fisher apparatus.

2.4.9 *In-vitro* Dissolution Studies

The drug release from lozenges was determined using USP dissolution testing apparatus type 2 (paddle method; Electro Lab, Mumbai). The dissolution test was performed using 900 ml of artificial saliva, pH 5.8 at 37 ± 0.5^{0}C and 50 rpm. A sample (10 ml) of the solution was withdrawn from the dissolution apparatus at different time intervals and the samples were replaced with fresh dissolution medium. The samples were filtered through a 0.45 µ membrane filter and diluted to suitable concentration with artificial saliva, pH 5.8. Absorbance of these solutions was measured at 225 nm using a Shimadzu UV/Vis double-beam spectrophotometer. Cumulative percentage drug release was calculated using an equation obtained from a standard calibration curve.

2.4.10 Stability Data

The optimized formulation B8 was subjected to stability studies, by storing at 40°C ± 2°C / 75% ± 5% RH for a period of 30 days.[14] At the optimized period, sample were evaluated for physical appearance, drug content, disintegration time and *in-vitro* dissolution studies.

2.4.11 Preliminary screening of Curcumin lozenges for antimicrobial activity

The *in-vitro* and *in-vivo* antimicrobial potential of compressed Curcumin lozenges had already been evaluated and published by authors. [15] The results indicated descent antimicrobial activity against selected set of pathogenic microorganisms.

3. RESULTS AND DISCUSSION

Curcumin powder was selected as an alternative to Ginger powder for throat infections and was found to be of standard grade and all excipients used in the study were found to meet the specifications as per I.P 2010. All the samples showed absence of sucrose. The granules were prepared in manner similar to that used for any compressed tablets.[16] The lozenge tablet differs from conventional tablet in term of organolepticity, non-disintegrating characteristics and slower dissolution profiles.[17]

The lozenges of final batch B8 showed smooth appearance and no cracks were found while inspecting using magnifying glass (5X and 10X) with very smooth flat surface and light orange yellow colour with aromatic fragrance with mild pungent taste and acceptable elegance. Lozenge thickness was almost uniform in all formulations and was found to be in the range of 3.0 mm to 3.28 mm. The hardness of each formulation was evaluated and found to be in acceptable range of 4.0 to 4.4 kg /cm^2.[9]

Wetting time is used as an indicator from the ease of the lozenge disintegration in buccal cavity. It was observed that wetting time of final batch B8 of lozenges was in the range of 15-32 seconds. The lozenge of optimized batch disintegrated in 90 Seconds which is acceptable for throat Lozenges. Disintegration time was within acceptance criteria of 1 minute to 1.5 minutes.

The drug content of the prepared lozenges was in the range and the correlation of variation was found to be less than 0.010%, indicating uniformity of the active ingredient in the prepared lozenges. Assay range was found to be 98.0% to 101.4%. Moisture content / water content were found within range of 1.70% w/w to 1.95% w/w.

The Stability Studies showed that Physical appearance remain unchanged. Assay value was unchanged within the limit 98.0% ± 2.0%. Dissolution was more than 95.0% in 30 minutes. Hardness, Thickness, Friability, Average Weight and Water Content were within the acceptance criteria. Disintegration time remained unchanged. From one month stability data, no significant change in parameters was observed indicating no degradation of active ingredient.

Table 2: Drug – Excipients Compatibility Studies

Ingredients	Ratio	Description	
		Initial	50^0C (3 weeks)
Curcumin powder	-	Light orange yellow color powder	NCC
Curcumin Powder + Mannitol	1:10	Light orange yellow color powder	NCC
Curcumin Powder + Microcrystalline cellulose	1:10	Light orange yellow color powder	NCC
Curcumin Powder + PVP K-30	1:5	Light orange yellow color powder	NCC
Curcumin Powder + Aspartame	1:1	Light orange yellow color powder	NCC
Curcumin Powder + Magnesium stearate	1:1	Light orange yellow color powder	NCC

NCC: No characteristic change

The drug and Excipients compatibility studies were performed by means of Physical mixture of drug and Excipients in different ratios (1:1, 1:1, 1:2.5, 1:3, 1:5, 1:10) at 50°C for three weeks and no characteristic change was observed. The results of physical observations of compatibility samples are depicted in table 2 above.

Drug-Excipients compatibility studies were also carried out using FTIR spectroscopy. The IR Spectra were recorded in between 400-4000 cm^{-1}. The FTIR spectrum of Curcumin matched as reported in literature [18]. The peaks obtained in the spectra of each formulation correlated with the peaks of drug spectrum. This indicated that there was no interaction of drug with excipients. Thus it could be concluded the drug was compatible with all the excipients.

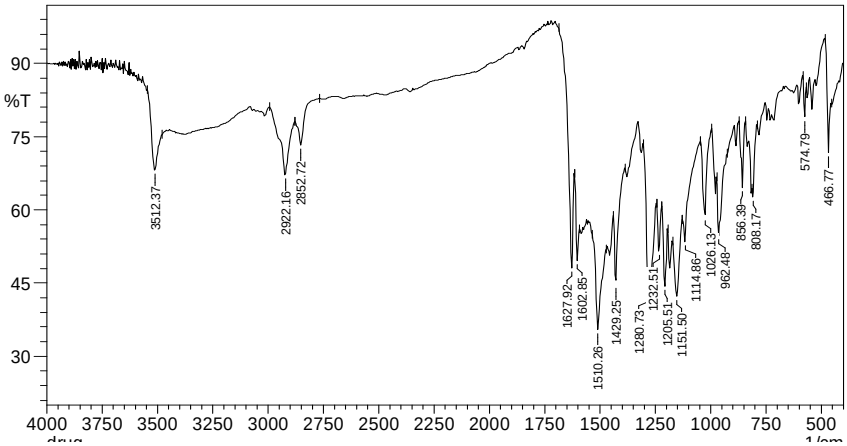

Fig. 1: FTIR of pure Curcumin

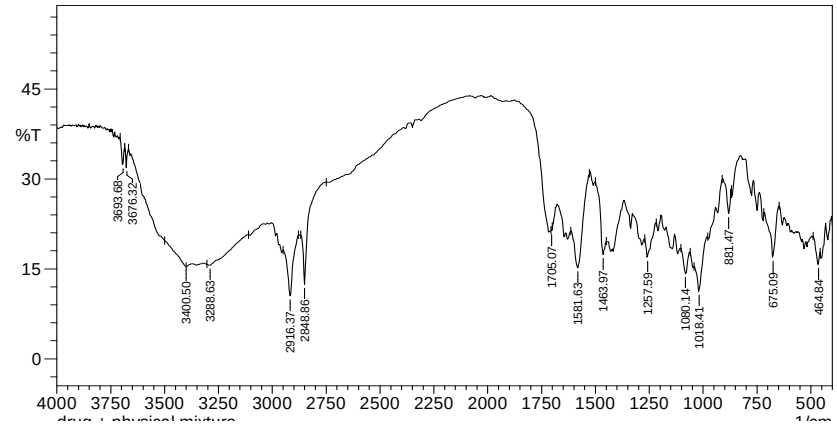

Fig. 2 : FTIR of physical mixture of all ingredients in formulation

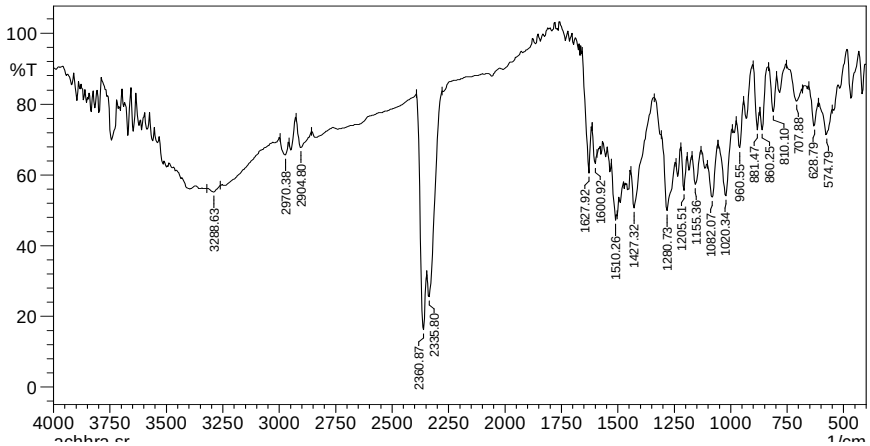

Fig. 3: FTIR of formulation (Curcumin lozenges)

Table 3: Pre-compression parameters for formulation

Formula	Angle of repose(Θ)	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Compressibility index (Carr's index) %	Hausner's ratio
B1	37.23 ± 0.02	0.581 ± 0.06	0.735 ± 0.04	20.95 ± 0 .40	1.26 ± 0.22
B2	32.21 ± 0.01	0.588 ± 0.05	0.757 ± 0.02	22.32 ± 0.36	1.28 ± 0.12
B3	29.24 ± 0.01	0.595 ± 0.03	0.769 ± 0.02	22.62 ± 0 .22	1.29 ± 0.23
B4	24.70 ± 0.03	0.602 ± 0.04	0.781 ± 0.08	22.91 ± 0 .21	1.29 ± 0.15
B5	20.8 ± 0.08	0.617 ± 0.04	0.806 ± 0.03	23.44 ± 0. 19	1.30 ± 0.12
B6	22.71 ± 0.01	0.641 ± 0.04	0.833 ± 0.02	23.04 ± 0 .17	1.29 ± 0.29
B7	39.69 ± 0.02	0.649 ± 0.03	0.862 ± 0.03	23.70 ± 0 .51	1.32 ± 0.98
B8	**42.8 ± 0.03**	**0.385 ± 0.04**	**0.454 ± 0.02**	**15.38 ± 0.22**	**1.18 ± 0.98**

The blends were evaluated for the parameters such as angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio. The angle of repose indicates qualitative and quantitative assessment of internal cohesive and frictional force under low levels of external loading as might be applied in mixing and tableting**.**[19]

The results of micrometrics properties were found to be within satisfactory limits. B8 formulation was selected for wet granulation method and compression was done using 15 mm punch size. The flow properties of the granules are essential as for as the handling and filling is concerned. The formula was optimized based on results of overall evaluation. The composition of final batch B8 is presented in table 1. The results of post compression parameters are summarized in tables 4 and 5.

Table 4: Post compression parameters of prepared Curcumin lozenges

Formula	Avg. weight (mg)	Thickness (mm)	Diameter mm	Hardness (kg / cm^2)	Friability (%)
B1	743.44 ± 0.12	3.01 ± 0.0005	14.95 ± 0.17	4.2 ± 0 .17	0.99
B2	733.94 ± 0.23	3.28 ± 0.0012	15.02 ± 0.02	4.0 ± 0 .12	0.39
B3	735.94 ± 0.12	3.20 ± 0.0031	15.03 ± 0.01	4.4 ± 0 .14	0.28
B4	744.94 ± 0.01	3.10 ± 0.0034	14.98 ± 0.02	4.2 ± 0 .02	0.20
B5	737.44 ± 0.25	3.15 ± 0.0051	14.99 ± 0.01	4.2 ± 0 .15	0.16
B6	722.94 ± 0.14	3.25 ± 0.0012	15.12 ± 0.01	4.1 ± 0 .10	0.15
B7	719.44 ± 0.28	3.18 ± 0.0005	15.22 ± 0.01	4.1 ± 0 .01	0.49
B8	**722.04 ± 0.12**	**3.0 ± 0.0005**	**15.00 ± 0.01**	**4.0 ± 0.01**	**0.19**

All the formulations were subjected to physical–chemical evaluations like weight variation, thickness, hardness, friability, drug content, disintegration test and wetting time were carried out in order to assess the suitability of the formulation with respect to the dosage form and intended therapeutic purpose. The average weight of each formulation was not maintained constant, but the weight variation was within ± 5% of variation. The hardness of each formulation was evaluated and found to be in acceptable range of 4 to 4.4 kg / cm^2. Lozenge thickness was almost uniform in all formulations and was found to be in the range of 3.0 mm to 3.28 mm. Friability was found to be less than 1% and considered to be satisfactory in the range of 0.15% to 0.99%.

Calibration curve of Curcumin

50 mg Curcumin powder was dissolved in 50 ml methanol to get 1000 ppm solution. 1 ml was pipetted from this and volume made up to 10 ml to get 100 ppm. From this solution, 1, 2, 3, 4, 5, 6 and 7 ppm solutions were prepared and absorbance of each solution was measured at 420 nm. The calibration curve was prepared.

Assay

20 tablets were powdered and the quantity equivalent to 20 mg Curcumin was weighed and dissolved in10 ml methanol and sonicated for 10 minutes. 1 ml of this solution was taken and volume made up to 10 ml with methanol. Absorbance of this solution was taken at 420 nm. Assay was performed in triplicate using calibration curve.

Table 5: Results of B8 batch

Expt. No.	Assay %	Mean
1	101.5 %	102.2 %
2	103.2 %	
3	101.9 %	

Table 6: Post Compression Parameters of prepared Curcumin lozenges

Formula	Disintegration time (sec)	Water content (w/w)	Assay (%)
B1	65±2	1.92±0.05	101.4±0.03
B2	62±3	1.90±0.09	98.7±0.01
B3	50±2	1.90±0.01	98.0±0.1
B4	42±4	1.84±0.17	100.5±0.18
B5	36±1	1.73±0.05	99.2±0.01
B6	38±3	1.71±0.5	99.3±0.03
B7	38±1	1.75±0.02	99.0±0.5
B8	**90±1**	**1.75±0.02**	**102.2.0±0.5**

The prepared Curcumin lozenges were evaluated for disintegration time, water content and assay. The results of all the test formulations were within the limit and passed. Assay range was found to be 98.0% to 102.2%. Disintegration time was within acceptance criteria up to 1.5 minutes. Water content by Karl fisher method was also within the range of 1.71% w/w to 1.92% w/w.

In-vitro Dissolution Study

The results of *In-Vitro* release profiles of different formulations are summarised in table 7.

Table 7: *In –Vitro* release profiles study of different formulations

Sampling time (minutes)	Drug release profile (% drug release)							
	B1	**B2**	**B3**	**B4**	**B5**	**B6**	**B7**	**B8**
10	80±0.90	82±0.52	82±0.43	85±0.24	84±0.23	86±0.28	86±0.90	86±0.90
15	84±0.82	88±0.85	86±0.56	89±0.51	87±0.29	90±0.35	87±0.82	89±0.82
20	93±0.28	91±0.68	90±0.76	92±0.73	90±0.40	92±0.73	93±0.54	93±0.54
30	95±0.58	93±0.72	95±0.23	94±0.04	94±0.20	96±0.26	92±0.29	98±0.29

In- Vitro drug release profile for all formulations were carried out by using artificial saliva (pH 5.8) as dissolution medium for 30 minutes. From the results obtained it was observed that the formulation B8 showed better release rate 98% within 30 minutes than other formulations. Hence, it was concluded that B8 was desired formulation and was taken for further stability studies.

Stability Data

The results of stability study of optimized formulation of Curcumin lozenges at accelerated conditions are summarised in table 8 to13.

Table 8: Physical and chemical parameters of Curcumin lozenges (B8) after 1 month at 40^{0}C ± 2^{0}C/75% RH ± 5% RH

Parameter	Initial	1 month
Description	Light orange to pale yellow, round shaped flat lozenges	No change
Average weight (mg)	722.04±0.12	No change
Hardness (kg /cm^2)	4.0	3.99
Thickness (mm)	3.0	No change
Friability (%)	0.19	0.17
Water content (w/w)	1.73	1.63
Assay	99.2	99.2

Packing: Blister pack

Table 9: Dissolution profile of Curcumin Lozenges (B8) after 1 month at 40^{0}C± 2^{0}C / 75% RH ± 5% RH

Time interval (min)	Drug release percentage (%)	
	Initial	final
10	86±0.90	86±0.25
15	89±0.82	89±0.21
20	93±0.54	92±0.15
30	98±0.29	96±0.85

Packing: Blister pack

Table 10: Physical and chemical parameters of Curcumin lozenges (B8) after 1 month at 40^{0}C ± 2^{0}C/75% RH ± 5% RH

Parameter	Initial	1 month
Description	Light orange to pale yellow, round shaped flat lozenges	No change
Average weight (mg)	722.04±0.12	No change
Hardness (kg /cm^2)	4.0	3.99
Thickness (mm)	3.0	No change
Friability (%)	0.19	0.17
Water content by KA (w/w)	1.73	1.63
Assay (% label claim)	99.2	99.2

Packing: HDPE Bottle

Table 11: Dissolution profile of Curcumin lozenges (B8) after 1 month at 40^{0}C± 2^{0}C / 75% RH ± 5% RH

Time interval (min)	Drug release percentage (%)	
	Initial	final
10	86±0.90	86±0.25
15	89±0.82	89±0.21
20	93±0.54	92±0.15
30	98±0.29	96±0.85

Packing: HDPE Bottle

Table 12: Effect of Temperature on hardness of lozenges

Storage temperature	Hardness (kg/cm^2)			
	1st week	4th Week	8th Week	12th Week
RT (28 ±2^{0}C)	4.0	4.05	4.05	4.05
37^{0}C	4.0	4.05	4.50	4.55
45^{0}C	4.0	4.06	5.51	5.50

Table 13: Effect of Temperature on Disintegration Time of Lozenges

Storage temperature	Disintegration Time (seconds)			
	1st week	4th Week	8th Week	12th Week
RT	90.0	90.0	90.2	90.2
37^{0}C	90.0	90.0	90.1	90.2
45^{0}C	90.5	90.5	90.8	90.8

Description remains unchanged. Assay value was unchanged within the limit 98.0% ± 2.0%. Dissolution was more than 95.0% in 30 minutes. Hardness, thickness, friability, average weight and water contents were within the acceptance criteria.

From one month stability data no significant changes in various parameters were observed in stability studies carried under accelerated conditions for optimized formulation B8.

Microbiological Evaluation

All raw materials used in final formulation B8 were tested for presence of Pathogenic microorganisms as per I.P. 2010 using below mentioned media.

Table 14: Results of microbial evaluation

Organism	Medium	Description of colony
Salmonella typhii	Xylose-Lysine-Desoxycholate agar	Red with or without black centers
Pseudomonas aeruginosa	Cetrimide agar	Greenish colony
Staphylococcus aureus	Mannitol-salt agar	Yellow colonies with yellow zones
Escherichia coli	MacConkey's agar	Pink colony
Yeast & Mold	Sabouraud dextrose agar with Chloramphenicol	--

All the samples of raw materials used in the formulations were tested for presence of selected set of pathogenic microorganisms and tests were found to be negative.

4. CONCLUSION

Based on the optimization of parameters it was felt that compressed lozenges of Curcumin herbal powder can be prepared by wet granulation method using mannitol as sucrose-free base. Several allopathic candy based lozenges for cough and cold are available in the market but contain high concentration of sucrose unacceptable for consumption by diabetic patients. The mannitol reportedly being metabolically inert in humans,[20] its lozenges may have vide acceptability among diabetics. These sucrose- free curcumin lozenges in addition to marketed Ginger lozenges may provide a suitable alternative to allopathic candy lozenges more acceptable to diabetics.

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