

Investigation of Organoleptic Characteristics in the Development of Soft Chews of Calcium Carbonate as Mineral Supplement

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The present study was aimed at developing a soft chewable dosage form for calcium carbonate for nutraceutical application. Two different types of the formulations *viz.*, sugar based and sugar free soft chews were prepared. The effect of various ingredients on the different organoleptic characteristics (grittiness, sweetness, hardness and mouthfeel) and the emulsion stability of the dosage form were checked and evaluated on the basis of an in-house numerical scale on healthy human volunteers. The study revealed that the type of emulsifying agent, heating temperature, particle size of the drug, ratio and quantity of sugars were found to have significant impact on the organoleptic characteristics of the dosage form. The study also indicates that the proper selection of packaging material is important in order to maintain the long term integrity of the formulation.

Key words—calcium carbonate; soft chewable dosage form; mineral supplement; sugar based; sugar free; evaluation method

INTRODUCTION

Most of the drugs given orally have bitter or non palatable taste,^{1,2)} which is the most common cause of non-compliance among patients.³⁾ Various methods such as drug particle coating,^{4,5)} encapsulation,⁶⁾ complexation⁷⁾ and chemical modification⁸⁾ have been utilized to mask the bitterness. However, these techniques are complex and extensive optimization is required for their practical application and, therefore, cost effective and simple taste masking technology needs to be developed.

Most commonly used method for masking the taste of the drug is to add masking agents to powders, liquids, mouth dissolving or chewable tablets.⁹⁻¹¹⁾ Chewable and mouth dissolving formulations are more suitable for paediatric and geriatric patients with a swallowing problem, over the liquid and powder forms which are difficult to handle. However, chewable tablets have additional advantage of high drug dose carrying capacity over mouth dissolving dosage form because of minimal requirement of superdisintegrants. Ideally, chewable formulations have smooth texture upon disintegration, pleasant taste and no bitter or unpleasant aftertaste. Upon chewing, they are broken down in the mouth and release their ingredients in the process and therefore, do not have

much lag time as required for the disintegration of tablets before absorption from stomach.¹²⁾

The various categories of drugs which may be incorporated as soft chewable drug delivery systems (SCDDS) are vitamins, mineral supplements, antacids, unpalatable drugs such as aspirin, ibuprofen, cimetidine, acetaminophen, erythromycin *etc.* These formulations can be readily chewed before swallowing without feeling the bitterness, unpleasant taste or odour of these unpalatable compounds. Mineral supplements (MS) available in the market as hard chewable tablets have a gritty mouthfeel and unpleasant aftertaste which can be overcome by formulating such ingredients as SCDDS for better taste and palatability.¹³⁾ Delivery of MS for treatment of mineral deficiency with the help of the soft chewable tablets can be helpful, specially to encourage children to easily accept MS in a tasty candy clothing. This dosage form also solves the dosage size problem which results from the higher dose of the MS. Therefore, the present work was designed to develop a SCDDS of a high dose MS, calcium carbonate (CC) with a pleasant mouthfeel and taste. The main objectives of this investigation were thus, to mask the grittiness and overcome the unpleasant taste of the drug, to optimize the quantities of the necessary excipients such as emulsifiers, oils and sugars to obtain a soft chew with optimum hardness and to optimize the processing conditions including temperature and stirring rate.

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MATERIALS AND METHODS

Materials The following materials were purchased and used as received. CC form Sigma Aldrich (Mumbai, India), Maltitol (MaltisweetMH80) from SPI Polyols Inc. (Delaware, US), Isomalt from Palatinit GmbH (Mannheim, Germany), Sucralose from Virchow Labs Ltd. (Hyderabad, India), Corn oil from Riddhi Siddhi Gluco Biols Ltd. (Ahmedabad, India), Milk Maid from Nestle India Ltd. (Gurgaon, India), Non-sweetened condensed milk from Ramson Dairy Products (New Delhi, India), Glyceryl monostearate (GMS) (Grade-Aracel 161) from Sandeep Medicose (Punjab, India), Polysorbate 80 from Johnson Matthey Chemicals (Chennai, India), Sorbitol liquid (Non crystallizing) from M/S Gulshan Polyols Ltd. (New Delhi, India) and Creamy vanilla flavour from Danisco Ingredients (Gurgaon, India). Other chemicals used were of analytical grade and were purchased locally.

Formulation Method The formulation was prepared in a stepwise manner as follows:

1. Preparation of O/W Emulsion GMS was melted in mixed vegetable oil by heating. CC in the required dose, was dispersed in water to form a slurry/paste and this slurry was added to oil phase with constant stirring at 1500 rpm to form a paste like w/o emulsion. A little excess water was then added to cause phase inversion of the emulsion to o/w type.

2. Preparation of W/O/W Emulsion Sugar was dissolved completely in minimum amount of

water with no crystal of sugar remaining undissolved followed by liquid glucose with isomalt dissolved in it. In case of sugar free formulation, isomalt, other polyols and sucralose were dissolved in water. Condensed milk with the required amount of emulsifier, Tween 80 or soya lecithin was added to the sugar syrup phase followed by salt (sodium chloride) for enhancing flavour. The mixture was heated with constant stirring till a light brown colour was obtained. Temperature was increased gradually and carefully to avoid the loss of excess water to reach the desired candy stage. The prepared o/w emulsion of step 1 was then added to it under stirring and the temperature was gradually increased till 121°–125°C to obtain the firm ball stage.

3. Preparation of the Soft Chew The prepared hot mixture of step 2 was poured into a stainless steel tray and cooled to room temperature. It was then kneaded like dough for graining the soft chew and was finally moulded and cut into pieces of required weight and shape to obtain the soft chew tablets. Graining is a process in which the sucrose crystals tend to aggregate to decrease the free movement of the molecules and improve the fracture and chewable property of the formulation.

The effect of various variables like ratio of sugar to L-glucose, GMS/Soy lecithin ratio, particle size of CC and heating temperature was studied on physical characteristics and palatability of sugar based formulations (Table 1) while effect of variables like amount of sucralose, Isomalt/MaltisweetMH80 ratio, sor-

Table 1. Composition of Batches for Sugar Based Formulations

Ingredients per chew (% w/w)	Bs1	Bs2	Bs3	Bs4	Bs5	Bs6	Bs7	Bs8	Bs9
Calcium Carbonate	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0
Sugar	23.0	28.0	33.0	28.0	28.0	28.0	28.0	28.0	28.0
Isomalt	12.0	12.0	12.0	12.0	12.0	12.0	12.0	12.0	12.0
L-glucose*	37.0	25.0	22.0	25.0	25.0	25.0	25.0	25.0	25.0
Sodium cholride	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Glyceryl monostearate	1.00	1.00	1.00	—	0.50	1.50	1.00	1.00	1.00
Mixed Vegetable Oil	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00
Condensed milk	15.0	15.0	15.0	15.0	15.0	15.0	15.0	15.0	15.0
Tween 80	—	—	—	—	—	—	0.05	0.10	0.15
Soy lecithin	3.00	3.00	3.00	—	3.50	2.50	—	—	—
Flavor	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Water**	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

Batches Bs10–Bs13 have same composition as that of Bs2. Particle size of batches Bs1–Bs9, Bs12 and Bs13 is 75 µm and that of Bs10 and Bs11 is 125 µm and 63 µm, respectively. The heating temperature for batches Bs1–Bs11 is 121–125°C and of Bs12 and Bs13 is 115–120°C and 126–130°C, respectively. ** Final water content of the soft chew should not be more than 10%. *Liquid glucose has 30% water and on heating this water evaporates leaving glucose as the sweetener.

Table 2. Composition of Batches for Sugar Free Formulations

Ingredients per chew (% w/w)	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10
Calcium carbonate	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0	18.0
Sucralose	0.015	0.025	0.035	0.025	0.025	0.025	0.025	0.025	0.025	0.025
Isomalt	27.0	27.0	27.0	32.0	22.0	27.0	27.0	27.0	27.0	27.0
Maltisweet MH80*	25.0	25.0	25.0	20.0	30.0	25.0	25.0	25.0	25.0	25.0
Sorbitol	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	3.00	10.0
Sodium chloride	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
Glyceryl monostearate	1.00	1.00	1.00	1.00	1.00	0.50	1.50	2.00	1.00	1.00
Mixed vegetable Oil	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00
Condensed milk	15.0	15.0	15.0	15.0	15.0	15.0	15.0	15.0	15.0	15.0
Tween 80	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10
Flavor	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Water**	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

In all the sugar free batches, the particle size of drug is 75 μm . B11 and B12 have same composition as that of B2. The heating temperature for batches B1–B10 is 121–125°C and of B11 and B12 is 115–120°C and 126–130°C, respectively. *Maltisweet MH80 has 25% moisture, 70% maltitol, 3% sorbitol, so percentage calculated on the basis of % w/w of the final formulation after heating. ** Final water content of the soft chew should not be more than 10%.

Table 3. Numerical Scales of Various Physical Evaluation Parameters of Soft Chewable Dosage Form

Physical Evaluation Parameters of Chewable Dosage Form			
Grittiness	Numerical value on Scale	Sweetness	Numerical value on scale
No gritty taste is observed	0.0	No sweetness	0.0
Grittiness cannot be detected unless carefully observed	0.5	Very low sweetness, not acceptable	0.5
Grittiness is not affecting the mouth feel	1.0	Sweetness is less and needs a little improvement	1.0
Grittiness can be observed in the soft chew but to a tolerable limit	1.5	Sweetness is proper	1.5
Grittiness is affecting the taste of the chew	2.0	High sweetness	2.0
Grittiness in the chew is reducing the sweetness and cannot be tolerated	2.5	Very high sweetness, bitter aftertaste	2.5
Hardness	Numerical value on scale	Mouthfeel	Numerical value on scale
Pourable liquid cannot be chewed and does not solidify	0.0	Poor, with grittiness	0.0
Highly viscous paste	0.2	Smooth but with grittiness	0.5
Soft mouldable, sticky and cannot be cut with knife	0.4	Smooth, pleasant	1.0
Moldable, can be cut with knife but becomes sticky at room temperature	0.6	Very smooth, melts in mouth	1.5
Soft and can be chewed and molded in desired shape	0.8	Separation of oil	Value on scale
Hard but can be chewed	1.0	No separation of oil	0.00
Very hard, rocky	1.2	Oil forms a thin layer on the surface of the chew	1.00
		Complete separation of oil	1.50

bitol and GMS concentration and heating temperature was studied in case of sugar free formulations (Table 2).

Evaluation Techniques

Evaluation of Physical Characters of the Formulation Taste evaluation of the soft chews was per-

formed by consensus of trained taste panel of the three age groups of healthy volunteers on the basis of feedback. The organoleptic properties of the tablets *viz.* grittiness, sweetness and mouthfeel and its physical property *viz.* hardness, were evaluated and rated according to an in-house numerical scale (Table 3).

The tablets were chewed in mouth for 60 s by each volunteer and the response was recorded using the numerical scale. After 60 s, the chew was spitted out and the mouth was rinsed thoroughly with mineral water.

CC Content Analysis Test solution was prepared by dissolving 10 soft chews in 400 ml water. 50 ml of concentrated hydrochloric acid was added followed by sonication of the sample to dissolve the carbonate salt. The mixture was heated on the hot plate and volume was made up with water and shaken vigorously. The solution was then filtered through Whatman filter paper (No. 1). 10 ml of the filtrate was taken and diluted to 100 ml. 15 ml of 0.1N NaOH solution was added along with the indicator, hydroxy naphthol blue. This sample was then titrated against 0.05M EDTA solution (previously standardized), to obtain a blue colored end point.

Mineral salt equivalent to elemental mineral (in mg/chew)

$$= \frac{\text{Volume of EDTA used} \times 2.004 \times M \times 1000}{(\text{no. of chews}) 10 \times 0.05 \times 10} \quad (1)$$

Similar solution prepared using dummy soft chews was used as blank. Batches B2 and Bs2 were analyzed for their drug content.

Drug Dissolution Study Dissolution study was carried out on six units using USP Dissolution Apparatus II using 900 ml of 0.1N HCl as dissolution medium maintained at $37 \pm 0.5^\circ\text{C}$ temperature and 50 rpm stirring rate. The tablets were first gently crushed using a mortar and pestle to mimic the *in vivo* chewing process and the powdered content (passing through sieve of A.S.T.M #20) equivalent to the weight of one tablet was then subjected to dissolution study. 10 ml of aliquots were withdrawn at predetermined intervals (15 and 30 min), filtered using Whatman filter paper (No.1) and the CC content was estimated titrimetrically.

Stability Studies To assess long term stability¹⁴⁾ of the prepared dosage form, formulations were packed separately in sealed high density polypropylene (HDPE) bottles and aluminium strips, and stored at $40^\circ\text{C}/75\%$ relative humidity (RH) in the stability chamber (Narang Scientific Works Pvt. Ltd., New Delhi, India) for 3 months. The samples were withdrawn at different time intervals (1, 2, and 3 months) and observed for their assay and moisture content using Karl fisher instrument (Metrohm, USA). The results were supported by statistical anal-

ysis using student 't' test and ANOVA (significance level $p < 0.05$).

RESULTS AND DISCUSSION

The success of a SCDDS is based on its ability to appeal the taste and mouthfeel of the patients. Unfortunately, no standard techniques are available to evaluate the characteristics specific to these kind of dosage forms. Therefore, the present investigation involving the development of soft chewable tablets was evaluated on the basis of an in-house numerical scale for rating the different organoleptic characteristics (grittiness, sweetness, hardness and mouthfeel) and the emulsion stability of the dosage form (Table 3).

Sugar Based Formulations

Effect of Ratio of Sugar to L-Glucose on Hardness

With the increase in the ratio of sugar/L-glucose at constant heating temperature (Batch Bs1, Bs2 and Bs3), the hardness of the final formulation increased (Fig. 1(A)). This is attributed to sugar which is solid in nature and has very low moisture content which imparts hardness while L-glucose has a higher moisture content imparting softness to the chew. Upon evaluation of these three batches, batch Bs2 was found to have optimum sugar to L-glucose ratio with respect to hardness, sweetness and mouthfeel. Therefore, moisture content of the excipients plays an important role in the overall hardness as well as it would also contribute to the long term physical stability of the product.

Effect of Heating Temperature on Hardness

Figure 1(B) shows that an increase in temperature from 120°C to 130°C increases the hardness considerably (batches Bs13) making the chew hard and rocky. At temperature below 120°C , the formed chew did not solidify on cooling and was very soft to be cut with knife (Bs12). At temperature beyond 125°C , the chew became harder and mouthfeel of the final formulation also became poor. Thus, the optimum temperature for making a soft chewable formulation was observed to be $121\text{--}125^\circ\text{C}$. This indicates that melting of sugar is critical and needs to be regulated carefully as heating beyond a certain temperature may result in change in the crystal lattice arrangement with increased crystal strength making them much harder than before.

Effect of Particle Size of CC on Grittiness and Emulsification Time

Figure 1(C) indicates a proportional decrease in grittiness with reduction in the particle size of CC. In addition, the emulsification

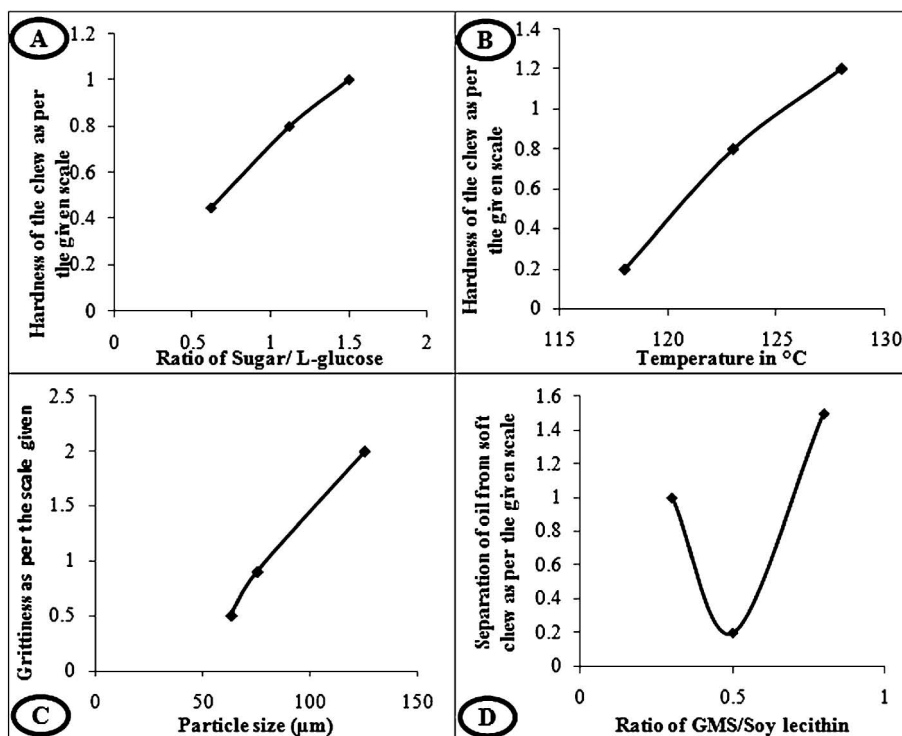


Fig. 1. Effect of Different Operating Variables on the Quality of the Sugar Based Soft Chewable Tablets

A: Effect of ratio of Sugar/L-glucose on hardness (Batches: Bs1, Bs2, Bs3), B: Effect of heating temperature on hardness (Batches: Bs2, Bs12, Bs13), C: Effect of particle size of CC on grittiness (Batches: Bs2, Bs11, Bs12), D: Effect of ratio of GMS/Soy lecithin on emulsion stability (Batches: Bs3, Bs5, Bs6).

time was also found to decrease with reduction in the particle size. This is because with reduced particle size, the surface area increases significantly which enhances the rate of contact of the drug particles with the surfactant solution. Drug of mesh size 125 μm and 75 μm showed emulsification time of 30 min and 15 min, respectively. With drug of mesh size 63 μm , grittiness was reduced but no significant reduction in emulsification time was observed. Therefore, 75 μm is the optimum size of CC with minimum grittiness and emulsification time. Further reducing particle size does not add much to the quality of the product. However, it would definitely increase its cost.

Effect of Ratio of GMS/Soy Lecithin on Emulsion Stability The increase in the ratio of GMS to soy lecithin from 0.3 (Batch Bs5) to 0.5 (Batch Bs2) resulted in a formation of a homogenous and uniform mixture without oil separation (Fig. 1(D)). However, with further increment in the ratio to 0.8 (Batch Bs6), the oil formed a thin layer on the surface of the final formulation, thus destabilizing the mixture and also imparting an oily taste and sticky feel to the chew. This may be due to the fact that with excess quantity of emulsifier a phase separation occurred. GMS is used as an emulsifier of low HLB value for

the preparation of initial w/o emulsion while soy lecithin is used as a stabilizer of the final formulation. As GMS itself imparts some taste to the formulation, therefore, its amount needs to be carefully regulated.

Sugar Free Formulations

Effect of Varying Amount of Sucralose on Sweetness Sucralose is a high intensity artificial sweetener which if added in excess results in bitter after taste. On increasing the concentration from 0.015% to 0.025% w/w, the sweetness of the formulation in batch B2 improved but on further increasing its amount to 0.035% w/w (Batch B3) resulted in a bitter after taste (Fig. 2(A)). The concentration of 0.025% w/w (Batch B2) was found to be optimum for imparting sweetness to the formulation in combination with other sweeteners.

Effect of Isomalt/MaltisweetMH80 Ratio on Hardness and Mouthfeel Variation in the ratio of Isomalt/MaltisweetMH80 ratio have an opposite effect on the hardness and mouthfeel of the chew (Fig. 2(B)). Low isomalt maltisweet ratio imparted sweetness, good mouthfeel and low hardness. Higher ratio resulted in conversion of a soft and viscous caramel to comparatively hard mass that could not be cut with knife. This indicates that Isomalt (a polyol in

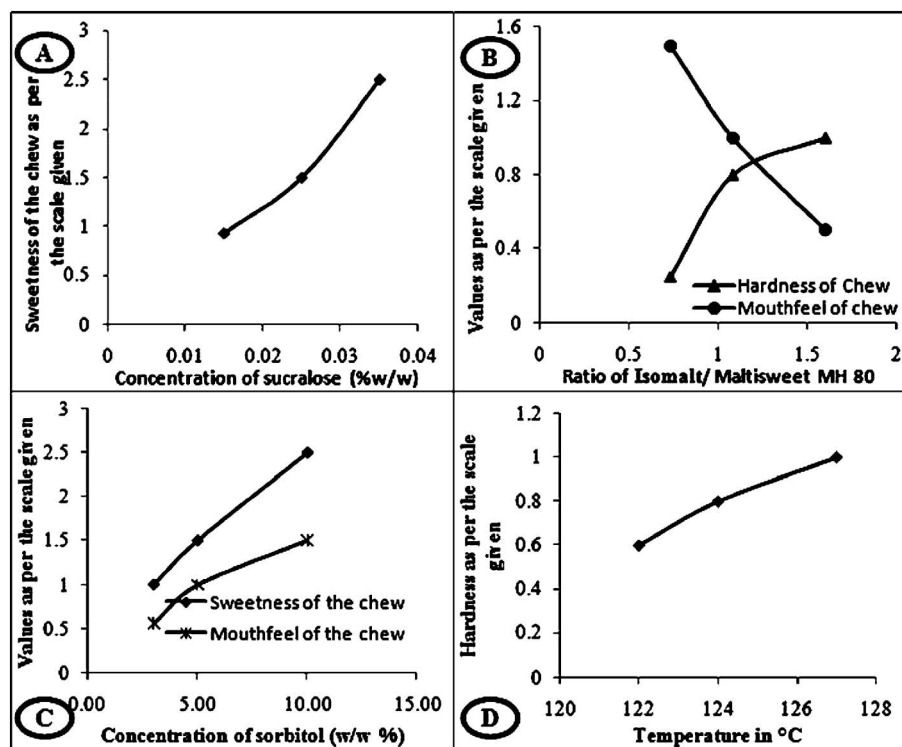


Fig. 2. Effect of Different Operating Variables on the Quality of the Sugar Free Soft Chewable Tablets

A: Effect of concentration of sucralose on sweetness (Batches: B1, B2, B3), B: Effect of ratio of Isomalt/MaltisweetMH80 on hardness and mouthfeel (Batches: B4, B5, B6), C: Effect of concentration of sorbitol on sweetness and mouthfeel (Batches: B8, B9, B10), D: Effect of heating temperature on hardness (Batches: B7, B11, B12).

powder form) plays an important role in providing hardness while MaltisweetMH80 (high molecular weight polyol with 25% moisture content) imparts sweetness and improves mouthfeel of the final formulation. From Fig. 2(B) it is clear that Isomalt/Maltitol ratio should be between 1.1–1.3 to obtain a product with optimum hardness and mouthfeel.

Effect of Sorbitol Concentration on Mouthfeel and Sweetness Sorbitol, a polyol was added to improve the mouthfeel and impart sweetness to the chew. However due to use of other sweeteners like isomalt, maltisweet and sucralose in the formulation, its concentration needs to be adjusted to achieve acceptable taste. An increase in the concentration of sorbitol from 3% w/w (Batch B9) to 5% w/w (Batch B2) was found to improve the mouthfeel and sweetness of the chew. However, at 10% w/w sorbitol concentration (Batch B10) the sweetness increased to an unacceptable limit (Fig. 2(C)).

Effect of Varying Temperature on Hardness

With increase in temperature during preparation, the hardness of the chew increased which may be due to decrease in the moisture content of the formulation. On increasing the temperature from 122°C

(Batch B13) to 124°C (Batch B2), the final formulation changed from viscous, soft caramel to a comparatively harder chewable caramel. However, on further increasing the temperature to 127°C the hardness increased considerably and also affected the taste of the formulation. Therefore, the optimum temperature range was found to be between 124°C–126°C (Fig. 2(D)).

Effect of Varying Concentration of GMS on Emulsion Stability Glycerol monostearate, an emulsifier is used to stabilize emulsions by preventing phase separation. As its concentration was increased from 0.5% (Batch B6) to 1% (Batch B2), the emulsion stability improved. A further increase in concentration of GMS to 1.5% (Batch B7) did not show any significant improvement in the stability of the formulation. However, an increase in GMS concentration to 2% (Batch B8) affected the taste of the formulation as GMS itself imparts an undesirable taste to the chew.

The complete evaluation of all the prepared batches revealed that batch Bs2 and B2 were having an optimum hardness, appreciable sweetness and mouthfeel and with low grittiness. Therefore, it can be inferred

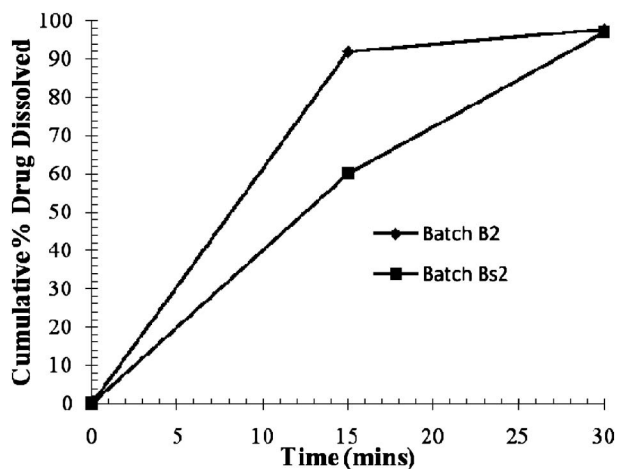


Fig. 3. *In-vitro* drug dissolution profile of optimized sugar based (Bs2) and sugar free (B2) batches

from the study that the choice and ratio of sugar/sugars (basic component of the formulation) and the processing temperature are the most significant parameters which require special attention in the development of a SCDDS.

CC Content Analysis The drug content in Batch Bs2 and B2 were found to be 490 mg 98% (490 mg) and 99% (495 mg), respectively, which was within the acceptable limit ($\pm 5\%$).

Drug Dissolution Study The dissolution study was conducted for Bs2 and B2. As can be seen from the dissolution profiles (Fig. 3), the CC was completely dissolved (100%) in 15 min in case of Batch B2 while in case of Batch Bs2, the complete dissolution of CC took place over a period of 30 min. This may be due to the fact that the hardened sugar present in Batch Bs2 dissolves slowly as compared to sugar free tablets which dissolves within few minutes.

Stability Studies The analysis of the stability samples indicated that the stability of the formulation was dependent on the type of packaging in which the samples were stored. Though the CC content and moisture content did not change in case of the samples packed in aluminium strips (data not shown), the HDPE bottle samples of sugar based chews showed a significant increase in the moisture level which resulted in distorted and sticky surface texture (Table 4). This may be due to lack of water resistance capacity of the HDPE bottles in addition to the hygroscopic nature of sugar. This indicates that aluminium packs are preferably better packing material for the SCDDS containing sugar as a major

Table 4. Stability Data of Optimized Sugar Based (Bs2) and Sugar Free (B2) Batches Packed in Sealed HDPE Bottles

Time	Sugar based formulation (Bs2)		Sugar free formulation (B2)	
	Assay	Moisture content	Assay	Moisture content
Initial	98.2	4.1	98.2	4.1
1 month	97.9	5.9	98.5	4.9
2 months	98.7	17.8	97.3	5.0
3 months	97.4	26.1	98.0	4.6

ingredient.

CONCLUSION

A mineral supplement of calcium was successfully formulated into a soft chewable dosage form (sugar based and sugar free) of desired taste, hardness and mouthfeel with low grittiness. The type of emulsifying agent, heating temperature, particle size of the drug, ratio of different sugars and quantity of sugars were found to have significant impact on the organoleptic characteristics of the dosage form. The proper selection of packaging material was also found to be important to maintain the long term integrity and stability of the formulation.

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