Research Article

A Novel Design Chewing Gum of Calcium Ions Isolated from Natural Source

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ABSTRACT

A pharmaceutical excipient includes calcium carbonate. It is widely used as a diluent in solid dosage forms. As a base for pharmaceutical and dental treatments, as a buffering and dissolution aid for dispersible tablets, as a food additive, and as a calcium supplement, this is utilised. Mineral salts, chiefly calcium carbonate, make up a significant percentage of the eggshell, accounting for around 95 percent of the shell. This Layer farm produces such a large amount of egg shells that their disposal is a problem for the environment. Oral drug delivery system researchers have created new formulations and technologies. The studies show the importance of the oral route among patients. There is an abundance of eggshells that are discarded by the food industry. Transformation of this waste into a pharmaceutical excipient. The conversion of this waste into pharmaceutical excipients will result in cost savings as well as a new supply of raw materials for chewing gum production. The goal of this research is to create eggshell powder as a calcium ion excipient in the production of chewing gum. To obtain a contamination-free material, the egg shells were first ground in a blender and then sterilized in a 20-litre horizontal digital stermax autoclave for 45 min at 122 °C. The egg shells were then ground into a fine powder in a Marconi MA 500 ball mill at 249 RPM for 12 hr. The ground eggshell powders were sieved in a No. 80 sieve (aperture of 0.177 mm) to limit particle size. Optical microscopy was used to examine the external morphology of powdered egg shells. Excipients improved the stability of the chewing gum while also enhancing medication release. The quicker the administration of the prescribed chewing gum begins, the better. Scanning electron microscopy was used to examine chicken eggshells with all excipients and pure eggshells (SEM). X-Ray Diffraction was used to examine the chicken eggshell with all excipients and pure eggshell (XRD). Pharmacopea specifications were used to evaluate all formulations. The pH, moisture content, viscosity, weight uniformity, And thickness tests were all within acceptable ranges.

Keywords: Chicken eggshell powder, Natural source, Calcium ions, Chicken eggshell Chewing gum, Chicken eggshell calcium carbonate.

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INTRODUCTION

Dental caries is defined as the acidic byproducts of bacterial carbohydrate fermentation causing localised damage to sensitive dental hard tissues. Microbial biofilm, which contains aerobic and anaerobic flora, covers the teeth surfaces. Streptococci and lacto bacilli are two mutants that are responsible for caries production due to their ability to produce acid when exposed to rapidly fermentable dietary carbohydrates such as sucrose, glucose, and fructose. This acid causes demineralization of inorganic constituents as well as the destruction of Organic constituents found in enamel and dentin.[1] When the body needs more metal (calcium), it takes it from places like the teeth. Dental issues such as weak roots, inflamed gums,

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brittle teeth, and cavities will arise as a consequence of this. The white spot lesion is the first visible sign of demineralization, which is caused by calcium Ion Loss. In India, most homes, hotels, and fast-food restaurants regard chicken eggshells as a waste material after using egg white and yolk. Due to tiny levels of other minerals, chicken egg shells are a simple natural source of calcium that delivers healthy, balanced calcium. Calcium carbonate, which is found in abundance in egg shells and is nearly 90% absorbable, is the greatest natural source of calcium. One teaspoon of the powder is made from one medium-sized chicken eggshell, which includes 750-800 mg of elemental calcium and other microelements. In osteoporosis patients and animals, eggshell powder has been found to boost bone mineral density.[2] Chewing gum has been a popular confectionery item since antiquity. In 2015, the global chewing gum market was estimated to be worth $ 25.8 billion in US dollars. According to a recent national consumer survey, approximately 56% of US households use chewing gum, with an annual consumption rate of 160 to 180 sticks per person.[3] In recent years, scientific and technological advances have been made in the search for and development of oral medicine delivery techniques. The ease with which the oral route may be administered is one of the reasons for its popularity. One of the most popular oral confectionery products is chewing gum. It has the potential to be a useful method of administering drugs to the oral cavity, both locally and systemically. Chewing gum has gained increasing acceptance as a drug delivery technique in recent years.[4] Chewing gums are solid or semi-solid pharmaceutical dosage forms that are combined with a water-insoluble gum basis and include one or more active pharmaceutical ingredients (API) and water-soluble or insoluble excipients. The medicine is intended to be chewed for a certain period of time in the oral cavity before the insoluble gum base is eliminated.[5] During chewing, the medication in the gum is released into the saliva. The medicine might be absorbed via the oral mucosa or make its way to the stomach for GI absorption. Both of these outcomes are, in fact, plausible. Chewing gum, as a consequence, has both a local and a systemic impact.[6] Absorption may happen in two ways with this medication delivery method. When medicine is absorbed directly via the buccal membrane, it bypasses the gastrointestinal tract's metabolism and, as a consequence, the likelihood of a first-pass action by the liver. As a consequence, chewing gum formulations may need a lower dosage than other oral medication delivery methods.[7]

MATERIALS AND METHODS

Materials

The Same sized chicken eggshells were collected from the chicken farm house. The eggshells were cleaned twice with distilled water, and then the eggshells were kept in a hot water bath at 100°C for 10 min for removing the pathogens and other impurities. Eggshells were dried in a hot air oven at 80°C for 2 hr. Then the egg shells were crushed using a mortar and pestle.

Methods

To obtain a contamination-free substance, eggshells were first mashed in a blender and then sterilized in a 20-litre horizontal computerized The Stermax autoclave for 45 min at 122°C. The eggshells were then ground into a fine powder in a Marconi MA500 ball mill at 249 RPM for 12 hr. To restrict particle size, the eggshell powders were sieved in a No.80 sieve (aperture of 0.177 mm) after grinding. The initial and the obtained material are Figure 1.

Calcium Ions from CESP

Determination of $CaCo_3$ in an eggshell

A major component of the eggshell is Calcium Carbonate ($CaCo_3$). This analysis was done volumetrically using a characteristic reaction of the carbonate compounds, namely a reaction with acids. Calcium Carbonate (chicken eggshell) is very insoluble in pure water but it will readily dissolve in the acid according to this reaction.

$2HCl\ (aq) + CaCo_3(s) \rightarrow Ca_2{+}(aq) + CO_2(g) + H_2O + 2Cl{-}(aq)$

The reaction is not used directly to the titrate $CaCo_3$ because it is very slow when this reaction was close to this endpoint. Instead of the determination being achieved by adding on this excess of acid to dissolve all of this $CaCo_3$ and titrating this remaining H_3O+ with NaOH a solution to the determination is an amount of acid with is not reacted with calcium carbonate. This difference between the amount of this acid (HCl) initially added to the continuously and the amount left over after this

Figure 1: Chicken egg shells (a) initial; and (b) powder obtained after milling and sieving.

Table 1: Weight and percentage of $CaCo_3$ present in CESP.

Egg sample	Weigh of calcium carbonate in grams	The percentage of calcium carbonate in eggshell
Chicken Egg Shell Powder	19.156	95.30%

Table 2: Preparation of CESP Chewing Gum (50gm).

Sl.no	Ingredients in (gm)	F1 (gm)	F2 (gm)	F3 (gm)	F4 (gm)	F5 (gm)	F6 (gm)	F7 (gm)	F8 (gm)	F9 (gm)	F10 (gm)	F11 (gm)	F12 (gm)
1	Eggshell powder	15	20	25	15	20	25	15	20	25	15	20	25
2	Glycerol	10	10	10	10	10	10	10	10	10	10	10	10
3	Sodium lauryl sulphate	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
4	Gum tragacanth	0.5	0.75	1.0	1.25	-	-	-	-	0.5	0.75	1.0	1.25
5	Xanthan gum	-	-	-	-	0.5	0.75	1.0	1.25	0.5	0.75	1.0	1.25
6	Calcitriol	0.75	1.00	1.25	1.50	0.75	1.00	1.25	1.50	0.75	1.00	1.25	1.50
7	Purified Water	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s

*Mean + SD (n=3)

reaction is equal to this amount used by the $CaCo_3$. This reaction is used to determine in a leftover acid is calcium carbonate. The results are shown in the Table 1.

HCl (aq) + NaOH (aq) → H2O + Na+(aq) + Cl-(aq)

Procedure for Calcium Ions from CESP

Clean the eggshells with water and dry them in the oven. By using a mortar and pestle. To make a powder form of the eggshells. In 100ml of the flask, add accurately weighed 0.50 g of eggshell powder were dissolved in several drops of ethanol (HCl can help to dissolve the eggshell but is not part of this reaction). Fill the burette with 0.1 M NaOH until it reaches the 0.0 ml mark. Allow the NaOH to drain into a small beaker until the solution reached the 0.0 ml point by opening the value. This beaker contains a little quantity of NaOH that may be thrown. Then add 2-3 drops of Phenolphthalein indicator. Titrate the eggshell sample until it becomes pink and remains that way for 30 sec to separate $CaCo_3$ from the eggshell.

Preparation of Chewing Gum (fusion method)

With the use of the pestle, eggshell powder, Calcitriol and xanthan gum are incorporated into a dry powder in a mortar and pestle. Glycerol, gum tragacanth and filtered water are then gently added to the dry powder while it is being mixed. The sodium lauryl sulphate excipients are then added at a predetermined time after this solution. After a succession of rollers shape the gum into a ribbon, it's ready to be sold The gum is kept cold for up to two days in a temperature-controlled environment. This ensures that the gum sets correctly. Final steps include trimming and cooling the gum in a temperature-and-humidity-controlled environment. The preparation table is shown in the Table 2, Figure 2 and 3 excipient details are shown in the Table 3.

Figure 2: Formulation of F11 Chewing Gum.

Formulation of Chewing Gum

Standard Curves For Calcium Carbonate

Preparation of Calibration medium

The calibration medium pH (6.8) was prepared by using phosphate buffer as per the IP procedure (I.P. 2014)

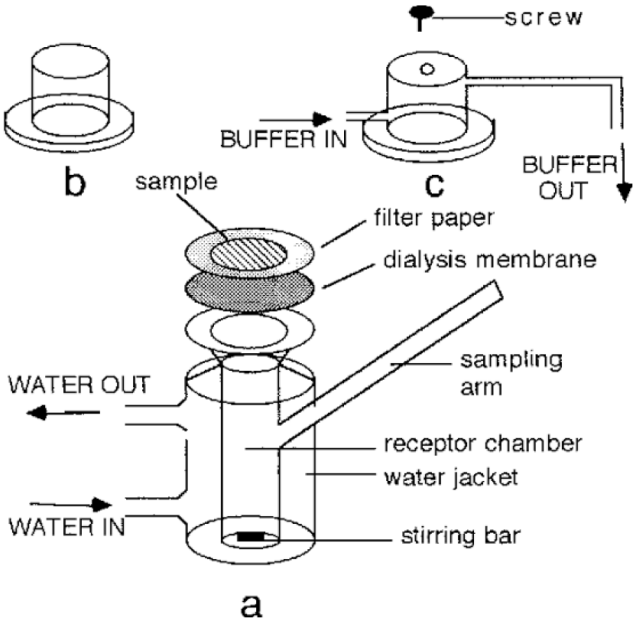

Figure 3: Schematic illustration of the Franz cell assembly in the standard [cover lid (b)] and in the modified [cover lid (c)] version.

Table 3: Selection of Excipients.	
Name of the excipients	**Use**
Calcitriol	Calcium-binding enhancer
Xanthan gum	Binder
Glycerol	Humectants
Sodium lauryl sulphate (SLS)	Glidant
Gum tragacanth	Binder

Determination of Maximum Absorbance (λ_{max})

The λ_{max} of Calcium Carbonate was estimated by scanning the 10µg/ml concentration of the drug solution in a buffer solution of phosphate pH 6.8. It showed the λ_{max} (Narendrachary, *et al.*, 2012) in a phosphate buffer solution of pH 6.8.

Preparation of Standard Curves

The standard curves of Calcium Carbonate were prepared by using phosphate buffer pH (6.8). The linear correlation coefficient was found to be 0.999 for pH (6.8) Calcium Carbonate obeys Beer's law within the concentration range of 2 to 10µg/ml. The results are shown in Table 4 and Figures 4-5.

Selection of Excipients

Infra-Red Spectrophotometric Analysis

1 g of Egg Shell was mixed with 100 g of dried potassium bromide powder to make the pellets. The mixer was then squeezed in a hydraulic press at 10-ton pressure to form a translucent pellet. To obtain IR Spectra, a thin pallet was placed atop a pellet disc. The results are shown in the Figure 6-7.

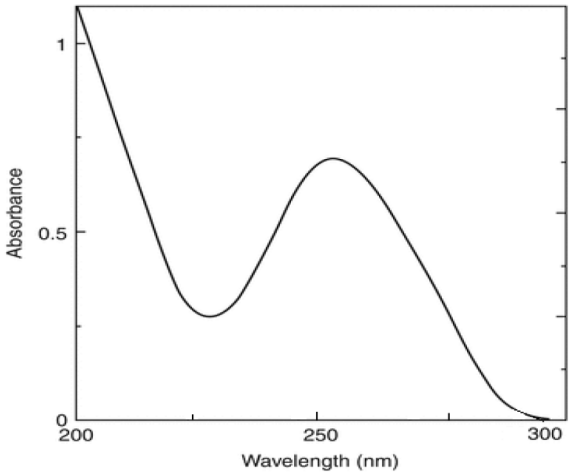

Figure 4: Determination of λ_{max} in calcium carbonate.

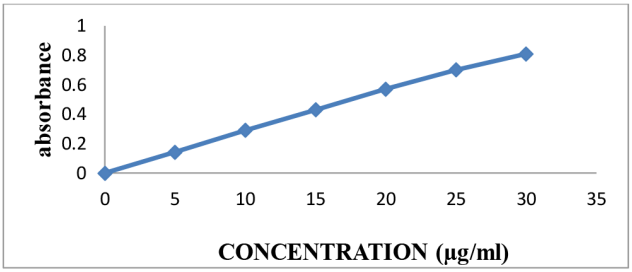

Figure 5: Preparation of Standard Curve.

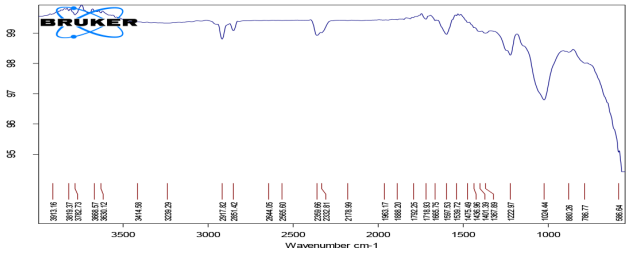

Figure 6: FTIR of the pure chicken egg shell.

Table 4: Calibration of calcium carbonate by using phosphate buffer ph– 6.8.		
Sl. No.	**Concentration (µg/ml)**	**Absorbance ± SD**
1.	5	0.1421 ± 0.010
2.	10	0.2901±0.016
3.	15	0.4289±0.022
4.	20	0.5712±0.051
5.	25	0.7003±0.048
6.	30	0.8101±0.053

*Mean + SD (n=3)

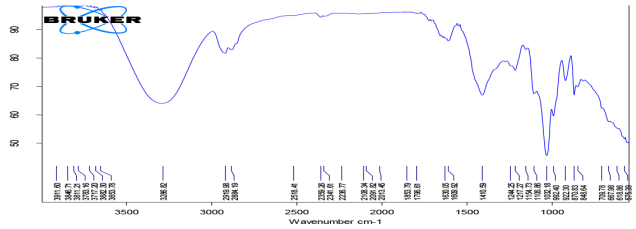

Figure 7: FTIR of eggshell powder and excipients.

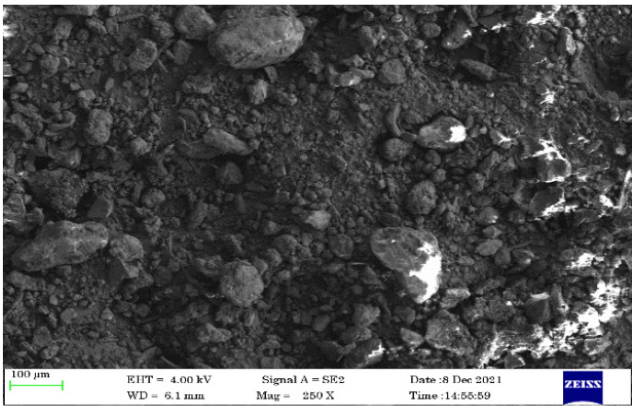

Figure 8: SEM Analysis of Pure Chicken Egg Shell Powder.

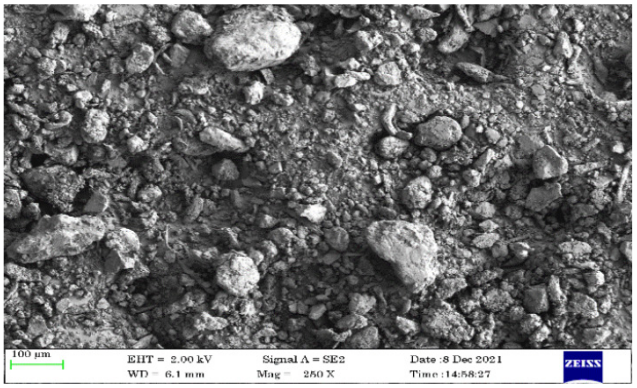

Figure 9: SEM Analysis of Pure Chicken Egg Shell Powder+Excipients.

Sem Analysis

Scanning electron microscopy (SEM) is one of the most widely used techniques for analysing surface morphology, such as spherical shape, smoothness and aggregate formation, and size distribution of (CESP) (Hitachi, Japan). CESP was dispersed onto double-sided tape and coated with 200 nm gold film under a decreased pressure of 0.001 mmHg before being affixed to aluminium stubs. The aluminium stub was inserted into a scanning electron microscope's vacuum chamber. Photographs were taken at a magnification that was appropriate. The results are shown in the Figures 8-9.

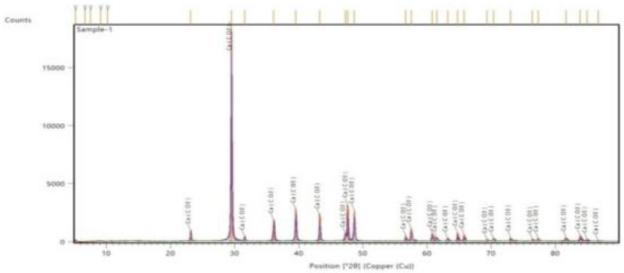

Figure 10: X-Ray Diffraction of chicken eggshell (calcium ion).

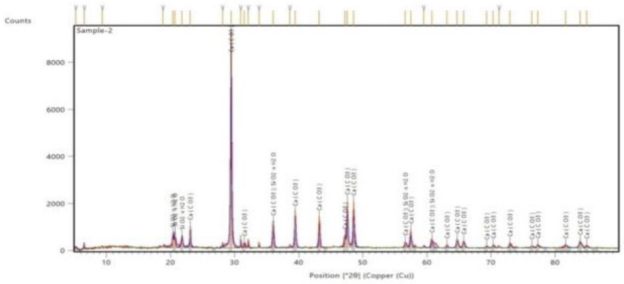

Figure 11: X-Ray Diffraction of chicken eggshell + Excipients.

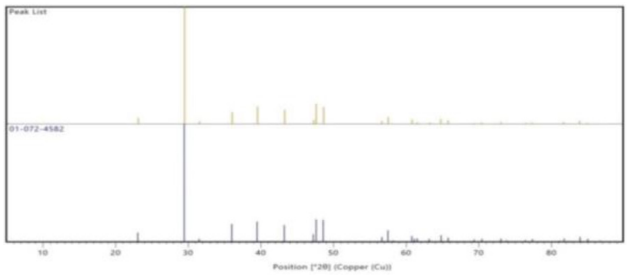

Figure 12: X-Ray Diffraction Matching Point of Chicken egg shell+Excipients.

X Ray Diffraction Studies

There is no resolution of interferences that correlate to the very long interplanar spacing that is common in natural materials when using standard X-ray diffraction equipment and technique. As a result, a new apparatus and method have been created in the University of Illinois' X-ray laboratory, which uses a magnetic field to deflect the dispersed electrons that normally fog the film. The results are shown in the Figure 10-12.

Preformulation Studies

Preformulation research refers to pharmaceutical and analytical research conducted before and in support of formulation development activities for a pharmacological substance's dosage form. Preformulation provides the foundational knowledge required to design a good formulation for calcium ions absorption. It provides information that is required.

Table 5: Preformulation Study of Egg Shell Powder.

Sl. No.	Parameters	Values	Observation
1	Bulk Density	0.268 gm/cm3	------
2	Tapped Density	0.321 gm/cm3	-----
3	Angle of Repose	300 11'	Excellent
4	Carr's Index	10%	Excellent Flow
5	Hausner's Ratio	1.37	Better Flow
6	Solubility		Insoluble inwater.

Table 6: Preformulation Study of the blend.

Batch Code (Powder Blind)	Bulk Density (gm/cm³)	Tapped Density (gm/cm³)	Angle Of Repose () *	% Compresibility*	Hausners Ratio*
F1	0.252	0.335	3114'	24.77	1.32
F2	0.223	0.344	30'	26.20	1.36
F3	0.232	0.335	29'	26.30	1.36
F4	0.234	0.334	28'	26.40	1.30
F5	0.243	0.354	32'	26.80	1.29
F6	0.245	0.335	30'	25.26	1.28
F7	0.263	0.332	30'	25.50	1.33
F8	0.264	0.321	30'	26.70	1.35
F9	0.277	0.345	30'	26.88	1.32
F10	0.282	0.353	30'	26.80	1.34
F11	0.294	0.363	30'	26.95	1.38
F12	0.274	0.354	30'	26.82	1.35

The following pre-formulation studies were performed on this obtained sample of the drug. The results are shown in the Table 5-6.

Evaluation of Chewing Gum

Organoleptic Parameter

the organoleptic properties of the formulated chewing gum were evaluated by their colour. (The visually colour was checked). Odour (found by smelling the product). Taste (checked manually by tasting the formulation). The results are shown in the Table 7.

Physical Characterization

Determination of pH

A total of 5 g of material was weighed and put in a 150 mL beaker. At a temperature of 27°C, 45 ml of newly boiled and cooled water was added to this. To form the suspension, it was thoroughly agitated. Using a pH metre, the pH of the sample was measured in less than 5 min.

Weight Uniform Test

According to the USP, a weight variation test is performed by weighing 12 different objects. Chewing gums are individually computing typical weights and comparing the weight of each chewing gum to the average. The weight variation test's result is presented as a percentage. This formula is often used.

$$\text{Weight variation} = (IW\text{-}AW)/AW \times 100\%$$

Where,

IW: Individual Weight

AW: Average Weight

Drug Content Test

The 10 chewing gums are chosen at random and their contents are measured; if each individual content is between 86 and 116 percent of the average content, it will pass the test; however, if any single preparation is outside of this range, it will fail the test.

Moister Content

5 g of the formulation is put in a porcelain dish with a diameter of 6-8 cm and a depth of 2-4 cm. Dry the sample in a 105°C oven.

$$\text{Moisture content (\%)} = W2\text{-}W3 \,/\, W2\text{-}W1 \times 100$$

where,

W1 refers to the weight of the container with the lid;

W2 refers to the weight of the container with the lid and the sample before drying;

W3 refers to the weight of the container with the lid and the sample after drying.

Study of Rhelogical Properties (Viscosity)

The viscosity of Chewing Gum was measured using a Brookfield digital viscometer (LV DV–II Ultras Programmable Remoter, USA) with a spindle no. 3 by raising the shear rate values in order to disclose the probable flow behaviour of this Chewing Gum. All viscosity tests were carried out at a constant temperature of 30°C.

In-vitro Diffusion Study

A conventional Franz diffusion cell (FDC40020FF, Crown Bio Scientific, Inc., Clinton, NJ) with a 20-mm aperture was utilised [It consists of a receptor chamber (a) (14.3 ml capacity), thermostated to 37°C by a water jacket, and a donor chamber (b), with a cover lid. The two chambers were separated by a 12,000-14,000MW cut-off dialysis membrane that had been cooked in distilled water for 15 min and thoroughly cleansed. A pH of 6.8 was maintained in the receptor phase. A phosphate

Table 7: Evaluation of Egg Shell Chewing Gum.

Sl. no	Evaluation test	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	Appearance	White	White	White	White	White	White	White	White	White	White	White	White
2	Weight uniformity test ± SD	996.1± 1.33	996.2± 0.08	996.2± 0.75	996.2± 1.34	996.6± 1.35	996.5± 1.43	996.3± 1.23	996.8± 1.33	996.7± 1.48	996.8± 1.38	996.9± 1.23	996.9± .1.33
3	Drug content in percentage ± SD	94.59± 0.63	94.57± 0.62	94.58± 0.76	94.6± 0.89	94.35± 0.21	94.33± 0.28	94.35± 0.67	94.36± 0.67	94.49± 0.65	94.59± 0.24	94.59± 0.12	94.6± 0.77
4	Moisture Content	15.66± 2.35	15.68± 2.80	15.68± 3.40	15.66± 1.43	15.56± 2.05	15.57± 3.01	15.59± 2.80	15.60± 2.42	15.70± 3.16	15.71± 2.30	15.0972± 4.39	15.71± 2.45
5	Viscosity	4567+ 118cps	4617+ 115 cps	4567+ 57 cps	4553+ 46.4 cps	5093+ 62.8 cps	5086+ 120 cps	5008+ 131 cps	5010+ 3115 cps	5433+ 89.3 cps	5597+ 137 cps	5833+ 120 cps	5398+ 120cps

*Mean + SD (n=3)

buffer of 0.1 M (KH2P04/NaOH) was employed. Prior to testing, the dissolved gas was removed from the receptor phase, and the receptor phase was agitated with a spin bar magnet throughout the test. Chewing gum (20 mg) was stacked on a paper filter disc before being placed on the dialysis membrane. At the filter disk-membrane and membrane-liquid interfaces, care was taken to prevent the production of air bubbles.

A clamp was then used to connect the donor chamber to the receptor chamber. Every 15 min, the fresh buffer was replaced with 0.5-ml samples taken by the sampling arm from the centre region of the receptor phase. The buffer replenishment was taken into account while calculating the cumulative Calcium Carbonate release. Spectrophotometrically, the drug in the receptor phase was detected at 254.91 nm. The results are shown in the Table 8.

Table 8: Percentages of Calcium Carbonate Release in a Diffusion Test Performed with the Franz Cell.

Formulation (chewing gum)	Time (min)			
	$CaCo_3$ releasing percentage			
	60	90	120	150
F1	7.25	11.52	12.88	14.41
F2	7.26	11.61	12.98	14.76
F3	7.26	11.67	12.98	14.81
F4	7.27	11.52	13.26	14.98
F5	7.9	12.06	14.38	16.46
F6	7.91	13.87	14.41	16.51
F7	7.91	13.79	14.42	16.67
F8	7.85	13.86	14.84	16.42
F9	8.12	14.58	15.6	16.62
F10	8.16	14.62	15.76	16.81
F11	8.24	14.98	15.98	16.65
F12	8.21	14.12	15.46	16.69

Release Kinetics Studies

Zero Order Kinetics

The following equation may be used to model drug dissolution from pharmaceutical dosage forms that do not disaggregate and release the drug slowly (assuming that the area does not change and no equilibrium conditions are established).

$$Q_t = Q_o + k_o t$$

Where,

Q_t = amount of drug released in time 't',

Q_o = initial amount of drug in the solution and

k_t = zero-order release constant.

This profile's pharmaceutical dosage forms release the same quantity of medication per unit of time, making it the best mechanism of drug release for achieving the long-term pharmacological effect. The drug dissolution of numerous kinds of modified-release pharmaceutical dosage forms, such as chewing gum, may be described using this relationship.

First Order Kinetics

Gibaldi and Feldman were the first to suggest using this approach in medication dissolving research. This model may be expressed using the following relationship:

$$\text{Log } Q_t = \text{Log } Q_o + k_t t/2.303$$

Where,

Q_t = amount of drug released in time't',

Q_o = initial amount of drug in the solution,

k_t = first-order release constant.

Pharmaceutical dosage forms that follow this dissolving profile, such as those containing water-soluble pharmaceuticals in porous matrices, release the drug according to the quantity of drug remaining in their

interior, such that the quantities of drug released per unit of time decrease.

Higuchi Model

Higuchi devised a number of theoretical models to investigate the release of water-soluble medicines embedded in semisolid and/or solid matrixes. The following equation may be used to explain the simplified Higuchi model:

$$f_t = k_H t^{1/2}$$

Where,

k_H= Higuchi diffusion constant,

f_t= fraction of drug dissolved in time't'.

Higuchi presents drug release as a square root time-dependent diffusion mechanism based on Fick's law. This relationship may be used for the dissolution of drugs from a variety of modified-release medicinal dosage forms, such as chewing gum.The procedure is shown in Table 9, and the results are shown in Table 10 and Figure 13-16.

Stability Studies

The stability test requirements are described in the International Conference on Harmonization (ICH) Guidelines under "stability testing of New Drug Substances and Products" (QIA). The results are shown in the Table 11.

In this research, the stability of the improved formulation was investigated 40°C±2°C/75%RH±5%RH for three months.

RESULTS AND DISCUSSION

Determination of Calcium Ions from Chicken Eggshell Powder

Determination of λ_{max} (UV Spectroscopy)

The UV spectrum of Calcium Carbonate in ethanol was scanned and λ_{max}. Were found to 254.91 nm.

Identification of Drug (EGG SHELL) Sample

The CESP was identified and confirmed by the FTIR spectrum. The Figure shows the FT-IR spectrum of Egg Shell. The characteristic absorption peaks of Egg Shell are within the pharmacopeia limits.

Table 9: ICH guidelines for the stability study.

Study	Storage condition	Time period
Long term	25vC±2°C/60%RH±5 RH OR 30°C±2°C/65%RH±5%RH	12 month
Intermediate	30°C±2°C/65%RH±5%RH	6 month
Accelerated	40°C±2°C/75%RH±5%RH	3month

Table 10: *In-vitro* Release Kinetics Data of Calcium Carbonate Chewing Gum.

Formulation code	Zero-order		First-order		Higuchi	
	r2	K0 (h-1)	r2	K1 (h-1)	r2	KH (h-1/2)
F1	0.998	2.611	0.813	-0.034	0.970	16.39
F2	0.969	2.723	0.823	-0.044	0.975	17.03
F3	0.986	2.746	0.798	-0.048	0.969	17.39
F4	0.967	2.703	0.902	-0.034	0.992	16.29
F5	0.985	2.805	0.864	-0.041	0.990	17.26
F6	0.968	2.816	0.853	-0.084	0.983	17.38
F7	0.995	1.821	0.794	-0.010	0.967	11.55
F8	0.997	1.970	0.817	-0.012	0.973	12.36
F9	0.983	2.016	0.796	-0.013	0.964	12.76
F10	0.998	1.904	0.829	-0.012	0.981	11.91
F11	0.998	1.946	0.796	-0.012	0.966	12.33
F12	0.987	2.036	0.794	-0.013	0.964	12.89

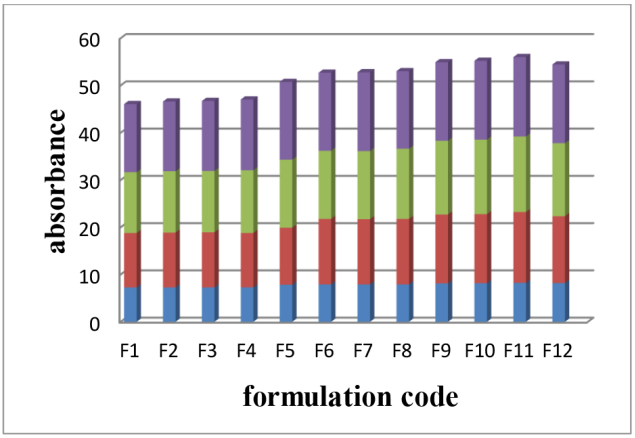

Figure 13: *In-vitro* diffusion Calcium Carbonate Releasing Study.

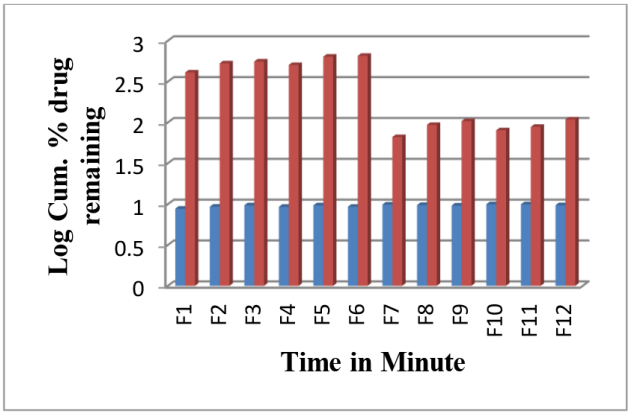

Figure 14: *In-vitro* Zero Order Kinetic Reaction.

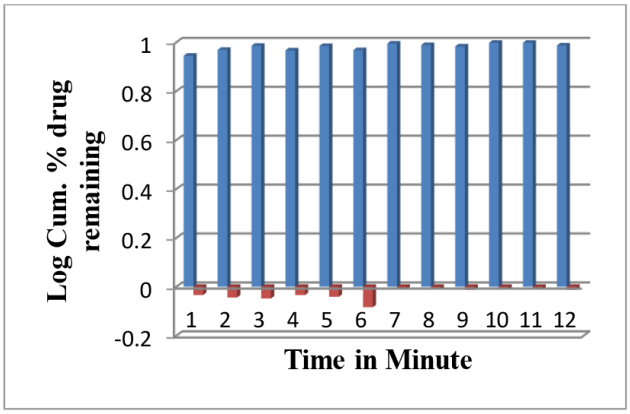

Figure 15: *In-vitro* First Order Kinetic Reaction.

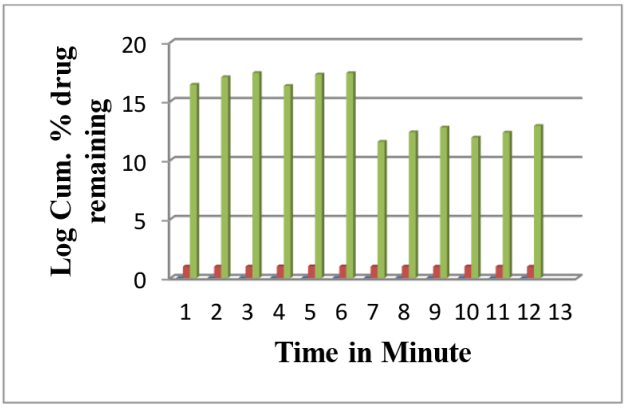

Figure 16: *In-vitro* Higuchi Order Kinetic Reaction.

Table 11: Stability studies of formulation F11 at an accelerated temperature of 40°C.

Parameters	Initial	After 45 days	After 3 month
Appearance	White	White	White
pH	6.8	6.8	6.8
Viscosity	5833±315 cps	5823±315 cps	5818±315 cps
Moisture content %	15.42	15.40	15.40
The drug content in percentage	94.59±0.12	94.55±0.12	94.550±0.12

Drug Excipients Compatibility Study

Compatibility of the CESP with excipients was determined by ATR-FTIR spectral analysis, this study was carried out to detect any changes in the chemical constitution of the drug after combining it with the recipients. The samples were taken for ATR- FTIR study.

Scanning Electron Microscopic (Sem) Analysis

X-Ray Diffraction

Preformulation Studies of Egg Shell Powder and Excipients

The Pre-formulation study relates to a pharmaceutical and analytical investigation to carry out the proceeding and supporting formulation in the development efforts of the dosage form of the drug substance. Various parameters of preformulation studies were calculated.

CONCLUSION

Based on the findings of the different assessment procedures, it was determined that an optimum controlled-release chewing gum formulation was created for the efficient and long-term absorption of calcium ions. Which was isolated from the shells of chicken eggs.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

ATR-FTIR: Attenated Total Reflectance- Fourier Transform Infrared; **CO_2:** Carbon dioxide; **HCl:** Hydro Chloric Acid; **H_2O:** Water; **Mm:** Milli meter.

SUMMARY

The present study is an attempt has been made to formulate in a medicated chewing gum of Calcium ions to achieve better patient compliance and improved drug release. In the present investigation, an attempt has been made to Chicken Egg Shell Chewing Gum by using different proportions of eggshell powder and different binder concentrations. The eggshell was made into fine powder by using a Marconi MA500 ball mill at 249 RPM for 12 hr. After grinding, the eggshell powders obtained were sieved in an No.80 sieve (aperture of 0.177 mm) for limiting particle size. The external morphology of the powdered eggshell was studied by optical microscopy.

The results of compatibility studies by infrared spectroscopy (FTIR), showed no interaction between the drug and stabilizers. Chicken eggshell with all excipients and pure eggshell was studied by Scanning electron microscopy (SEM). Chicken eggshell with all excipients and pure eggshell was studied by X-Ray Diffraction (XRD). The two matching peaks of pure eggshell powder in 30 positions [20] (copper [Cu]) is $CaCo_3$ is counting value is a 2000 and pure eggshell powder and

excipients in 30 positions [20] (copper [Cu]) for calcium carbonate was found for pure eggshell powder. The various components and different formulations.

In the assay, results were shown for each 20g of CESP as a percentage of calcium carbonate was 95.30%. Preformulation studies were carried out; the organoleptic properties complied with the Pharmacopeial specification. Physical properties such as bulk density the best formulation (F11) was found to be 0.294 gm/cm^3 and tapped density the best formulation (F11) was found to be 0.363 gm/cm^3, angle of repose the best formulation (F11) was found to be 30º55', % compresibility the best formulation (F11) was found to be 26.95. Hausner ratio the best formulation (F11) was found to be 1.38 were within the limits.

In the optimized formulation (F11) no significant change was observed in content uniformity, physical properties and absorption rate, after the storage period of 3 months at 40ºC and 75%RH.

The *in-vitro* Studies of Calcium Carbonate Released in a Diffusion Test Performed with the Franz Cell formulation (F11) was slowly a controlled release character, Which was very prominent than compare to other formulations.

Disclaimer

In our field of study and country, the goods employed in this study are commonly and majorly used. Because we do not intend to use the items as a tool for litigation, but rather to enhance knowledge, there is no conflict of interest between the authors and the manufacturers of the products. Furthermore, the research was funded solely by the writers' own efforts, rather than by the production company.

Ethical Approval

Written ethical approval has been gathered and retained by the author in accordance with international or university standards.

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