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Design, Development & Evaluation Of Cilnidipine Bio-Adhesive Sustained Release Tablets Using Natural Gum

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Abstract : Bio-adhesive sustained release tablet is a potential approach of GRDDS. Cilnidipine is an L/N type dihydropyridine 4th generation calcium channel blocker (CCB), which decreases hypertension by blocking the N-type calcium channel to attenuate vascular sympathetic neurotransmission. It has high first-pass metabolism leading to low bioavailability. Hence the present research work was undertaken to formulate bio-adhesive sustained release tablet of Cilnidipine with an objective to enhance therapeutic efficacy, bioavailability. Here in this study we have taken different natural gums like Sersuan, Rahen, Kekat, Sahaj, Albujia, Char and Tal as natural bio-adhevise polymer. Kekat show maximum bio adhesive strength. Final Clinidipine bio-adhesive tablet have prepared by taken kekat in different concentration. Optimise formulation has evaluated.

***Key Words*:** Cilnidipine, Bio-adhesive, natural gums, Dissolution

I. INTRODUCTION

Oral administration is the major route for drug delivery. Oral controlled release systems are used for controlled action of active ingredients to the targeted site. But oral controlled release systems have many problems such as first pass hepatic metabolism, enzyme degradation, swallowing problem etc. Bioadhesion is defined as an ability of a material to adhere to a biological tissue for an extended period of time. In case of polymer, it attach to the mucin layer of a mucosal tissue, the term mucoadhesion is used. Adhesion may be defined simply as a process of "fixing" of two surfaces to one another.So, as compared to oral controlled release systems, mucoadhesive delivery system have several advantages like prolongation of residence time, drug targeting, intimate contact between dosage form and the absorptive mucosa. In addition, mucoadhesive dosage forms have been used to target local disorders at the mucosal surface to reduce dose and to minimize the side effects. Mucoadhesive formulations use polymers as the adhesive component.

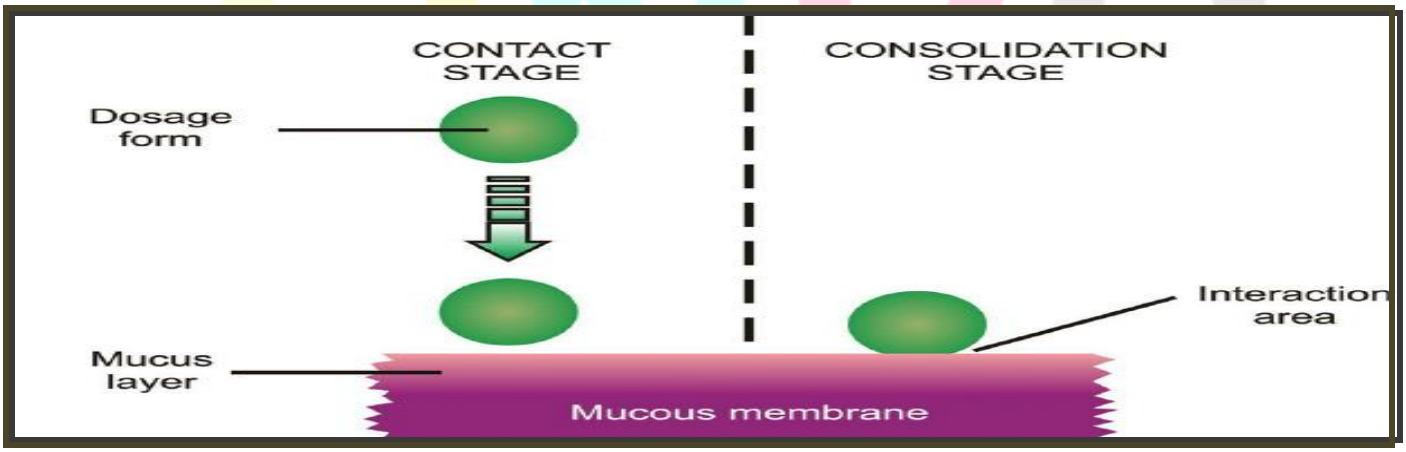

Figure 1.1: The stages of adhesion on mucous membrane

High blood pressure (hypertension) is a common condition in which the long-term force of the blood against your artery walls is high enough that it may eventually cause health problems, such as heart disease.

Blood pressure is determined both by the amount of blood your heart pumps and the amount of resistance to blood flow in your arteries. The more blood your heart pumps and the narrower your arteries, the higher your blood pressure. A blood pressure reading is given in millimeters of mercury (mm Hg). It has two numbers.

Top number (systolic pressure). The first, or upper, number measures the pressure in your arteries when your heart beats.

Bottom number (diastolic pressure). The second, or lower, number measures the pressure in your arteries between beats.
You can have high blood pressure for years without any symptoms. Uncontrolled high blood pressure increases your risk of serious health problems, including heart attack and stroke. Fortunately, high blood pressure can be easily detected. And once you know you have high blood pressure, you can work with your doctor to control it.

II. MATERIALS & METHODS

2.1 Preformulation Studies

Preformulation testing is the first step in the rational development of dosage form. It can be defined as an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. The overall objective of preformulation studies is to generate information useful to the formulator in developing stable and bioavailable dosage forms, which can be mass-produced

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2.1.1 Identification of Drug

2.1.1.1 Melting Point Study

Melting point of Cilnidipine was determined by using the capillary tube method using melting point apparatus.

Differential scanning calorimetry (DSC) studies

The melting point study was carried out with the help of Differential scanning colorimetry (DSC). Samples (2-3 mg) were placed in flat bottomed aluminum pan and heated at a constant rate of 10°C/min in an atmosphere of nitrogen in a temperature range of 20–300°C.

2.1.1.2 FTIR Absorption Spectroscopy Study

The infrared spectra were recorded using FTIR according to the KBr disc technique. The FTIR measurements were performed in the scanning range of 4000– 300 cm^{-1} at ambient temperature.

2.1.1.3 Spectometric Analysis of Cilnidipine

Stock solution for Cilnidipine:

10mg of cilnidipine was accurately weighed and transfer to a 10ml volumetric flask and volume was made upto 10ml with Methanol (stock solution A – 1000ug/ml). Form stock solution A 1ml was taken into a 10ml volumetric flask and volume was made upto 10ml with Methanol (stock solution B – 100ug/ml).
Standard stock solution of cilnidipine was scanned for absorbance between 200-400 nm by means of double beam UV Visible spectrophotometer. The solution will be scanned in the range of 200 to 400 nm to fix the maximum wave length and UV spectrum can be obtained.

2.1.1.4 Procedure for Standard Calibration curve:

Standard solution of cilnidipine in concentration range of 2 µg/ml to 10 µg/ml, obtained by transferring (0.2, 0.4, 0.6, 0.8, 1.0 ml) of cilnidipine stock solution (100 µg/ml) to the series of 10 ml volumetric flask. All dilution scanned in wavelength range 200 nm to 400 nm.

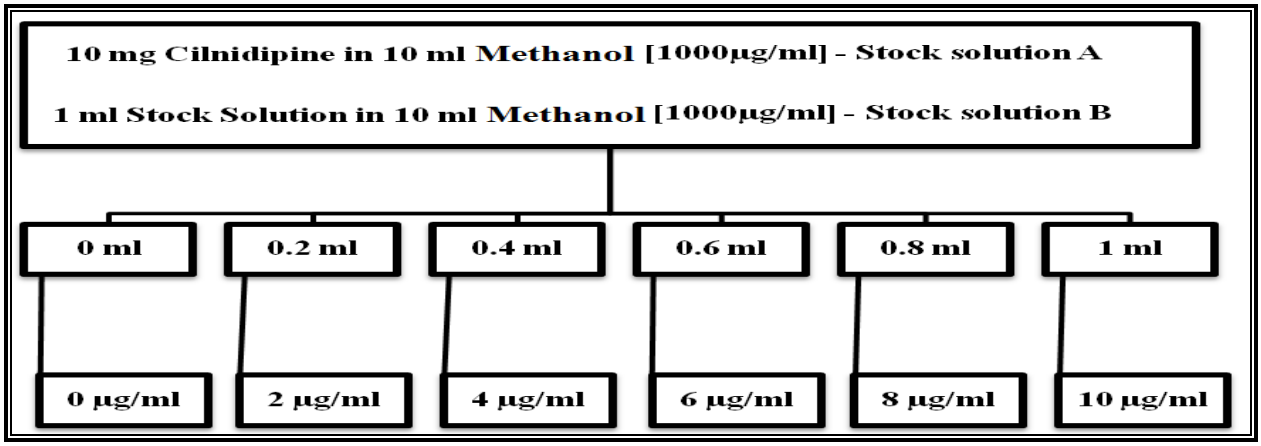

Figure 2.1: Preparation of standard solution

2.1.2 Organoleptic Properties

The color, odour, and taste of the drug were characterized and recorded using descriptive terminology.

2.1.3 Solubility studies

Solubility is a useful parameter mainly for poorly soluble drugs. Bioavailability problems are often present, when the solubility of a drug is less than 10 mg/ml over the pH range 1-8. Drug solubility will be determined by preparing saturated drug solutions in various medium, maintained at 37°C ± 0.5°C in a water bath and continuously shaken in to mechanical shaker up to 24 hrs. Withdrawn samples will be filtered through a filter paper, and assayed by UV spectrophotometer.

2.1.4 Micromeritic properties evaluation

For determination of flow properties of formulations we perform different parameters like Bulk Density, Tapped Density, Carr's Index [Compressibility Index, Angle of repose.

2.2 Collection, Extraction and Isolation

Collection of gum exudates by tapping method and initially exudates were sticky and colorful according to plants, became harder and darker after two weeks and it was cleaned by removing the external bark and other extraneous materials by hand, finally dried in hot air oven at 50°C until it become sufficiently brittle. It was powdered by using Mortar-pestle and sifted through the sieve No.100 (nominal mesh aperture size 75 µm and approximate % sieving area 36). It was dispersed in distilled water in the proportion of one part of plant material to ten parts of the water. The extraction continued for 24 hrs at room temperature with continuous stirring using stirrer. The supernatant was separated by muslin cloth. The final residue was washed with water and washings were added to the supernatant. The procedure was repeated three times. The supernatant was collected and treated with twice the volume of acetone to isolate the gum by continuous stirring and it was separated by centrifugation process. The formed precipitate was washed with acetone and dried at 40-50°C in hot air oven. The dried gum was pulverized by laboratory blender and passed through sieve No.100. It was stored in tightly closed container and kept in a desiccator. The percentage yield was calculated by the following equation.

Percentage yield = W_1 / W_2 X 100

Where, W1 weight of crude exudates, W2 weight of the isolated gum.

This common procedure is followed for collection, extraction and isolation of Sersuan, Rohen, Kekat, Sahaj, Albujia, Char and Tal gum.

Table 2.1: Scientific name of different Natural Gums

Natural Gum	Scientific Name
Sersuan	Albijia lebbeck
Rahen	Soyamedia febrifuza
Kekat	Acacia Karoo
Sahaj	Terminalia Elliptica
Albujia	Albizia gummifera
Char	Buchanania Lanzan
Tal	Borassus Flabellifera

2.3 Method of Preparation of different Natural Gum Tablets

Natural Gum tablets were prepared by using direct compression technique. In this research work all seven types of gum were used and different formulations were prepared. Here all natural gums were used in same concentration to find out there bio-adhesive capacity. Other excipients like diluent, binder, lubricant and anti-adherent were used. All seven formulations are given in the following table.

Table 2.2: Formulations of Natural Gum Tablets

Formulation Qty (mg / Tab)							
Ingredient	**Sersuan**	**Rohen**	**Kekat**	**Sahaj**	**Albujia**	**Char**	**Tal**
Gum	70	70	70	70	70	70	70
MCC	120	120	120	120	120	120	120
Magnesium Stearate	4	4	4	4	4	4	4
Aerosil	4	4	4	4	4	4	4
Talc	2	2	2	2	2	2	2
Total weight	200	200	200	200	200	200	200

2.4 Post-compression Evaluation of Natural Gum Tablets

2.4.1 Weight Variation

Twenty tablets will be weighed individually and the average weight will be determined. The % deviation will be calculated.

2.4.2 Tablet Hardness

The resistance of tablet for shipping or breakage, under conditions of storage, transportation and handling, before usage, depends on its hardness. The hardness of tablet of each formulation will be measured by Monsanto hardness tester.

2.4.3 Determination of Bio-adhesive strength of the Natural Gum Tablets

The force required to separate the sample disk from model substrate were measured using a modified balance method. The formulation was fixed to the one side of the balance and come into contact with mucosal membrane of sheep or goat stomach, the tablets were left for 5 min for hydrate. A beaker was place on a moving platform. The beaker was then slowly raised until the substrate come in the contact with the formulation. On the other side of the balance fractional weight was added at a constant rate. The addition was stopped as soon as the detachment of formulation from the surface of mucosal membrane was obtained.

The weights required for complete detachment was measured and expressed as bio-adhesive strength. Procedure was repeated for three more time for formulation. Average was recorded.

Calculation of the force of adhesion from the bio-adhesive strength.

Force of adhesion (F) = [W x g] / 1000 ..... (4.3)

Where,

F = Force of adhesion in N

W = Bioadhesive strength in g

g = Acceleration due to gravity

This common procedure is followed for the determination of bio-adhesive strength for all seven Natural Gum Tablets.

2.4.4 Acute Oral toxicity study of the optimise gum *Acacia Karoo* (Kekat)

The acute toxicity of gum was determined as per organization for economic co-operative and development (OECD) guidelines No. 425. In acute toxicity study, determination of LD50 was carried out in healthy albino mice of either sex. Albino mice were fasted over night, the fasted body weight of each animal was determined and dose was calculated according to the body weight. Animals weighing 160–200 g was randomly divided into 7 groups comprising of five animals each. The control group received normal saline (10 mL/kg per oral) and other groups received 100, 200, 500, 1000, 1500 and 2000 mg/kg of *Acacia Karoo* (Kekat) dispersion in distilled water. The animals were observed continuously for the behavioural changes for first 30 min after dosing and observed periodically (with special attention given during the first 4 hrs) for the next 24 hrs and then daily thereafter, followed for 14 days. All observations (changes in skin and fur, eyes and mucous membranes and behavioural pattern) were systematically recorded with individual records being maintained for each animal. Special attention was given for observation includes tremors, convulsions, salivation, diarrhoea, lethargy, sleep, coma and mortality. Observations and changes (if any) in wellness parameters were compared with that of control animals. The individual body weights of animals were recorded before the administration of drug on 1st day of the study and thereafter on the 7th and 14th day of the experiment. Observations in the body weight of individual animals were noted and compared with that of the control animals.

2.5 Method of Preparation of Sustained Release Tablets of Cilnidipine

Cilnidipine matrix tablets were prepared by using direct compression technique. In this research work there are five different formulations were prepared. Here optimize gum ***Acacia Karoo* (Kekat)** was use in different concentration to show the bio-adhessive property as well as retard the drug release. Other excipients like diluent, binder, pH modifier, lubricant and anti-adherent were used. All five formulations are given in the following table.

Table 2.3: Formulations of sustained release tablets of cilnidipine

Formulation Code (Qty mg/tab)					
Ingredient	**CLN 1**	**CLN 2**	**CLN 3**	**CLN 4**	**CLN 5**
Cilnidipine	10	10	10	10	10
Gum	40	60	80	100	120
MCC	130	110	90	70	50
$NaHCO_3$	10	10	10	10	10
Magnesium Stearate	4	4	4	4	4
Aerosil	4	4	4	4	4
Talc	2	2	2	2	2
Total weight	200	200	200	200	200

2.6 Determination of flow property

Different micromeritics properties like Bulk Density, Tapped Density, Compressibility Index, Hausner's Ratio, Angle of repose were determined to find out the flow property.

2.7 Procedure for tablet preparation

Weighing and Shifting

1) All the ingredient were weighed accurately, according to their respective weight.
2) Cilnidipine and remaining excipient passed through sieve no #40.

Lubrication

Dried granules were blended with Mg. stearate, aerosol and talc for 10 minute in a double cone blender.

Compression

Lubricated granules were compressed by 06 mm circular punch (standard concave)

2.8 Post-compression Evaluation of bio-adhesive matrix tablets

2.8.1 Tablet thickness

Thickness of tablets is an important for uniformity of tablet size. Thickness will measure by using Vernier Calipers on 3 randomly selected samples.

2.8.2 Tablet Hardness

The resistance of tablet for shipping or breakage, under conditions of storage, transportation and handling, before usage, depends on its hardness. The hardness of tablet of each formulation will be measured by Monsanto hardness tester.

2.8.3 Friability

Friability is the measure of tablet strength. Roche friabilator is will be taken in use for testing the friability using the following procedure. Twenty tablets will be weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min., the tablets will be weighed and the percentage loss in tablet will be determined.

$$\% \text{ loss} = \frac{\text{Initial wt. of tablets} - \text{Final wt. of tablets}}{\text{Initial wt. of tablets}} \times 100 \quad \text{.....(4.1)}$$

2.8.4 Weight Variation

Twenty tablets will be weighed individually and the average weight will be determined. The % deviation will be calculated.

2.8.5 Uniformity of Content

Content of active ingredient in tablets will be taken at random, will be determined. 10 tablets will be weighed and average weight will be calculated. All tablets will be crushed and powder equivalent to 10 mg will be dissolved in 100 mL methanol and 1 mL of this solution was diluted to 10 mL with methanol and measured spectrophotometrically at λmax of 240 nm against reagent blank. Amount of drug present in one tablet will be calculated.

2.8.6 Swelling Study

The swelling behavior of tablet described as the water absorbing capacity. The tablets will be weighed individually (W_0) and placed separately in petridis containing cellophane membrane and incubated at 37 ± 1^{0}C. At regular time intervals until 18 hours, the tablets will be removed carefully. The swollen tablet will be then reweighed (Wt) and the % swelling will be calculated using the following formula:

$$\textbf{\% swelling} = \{(W_t - W_0)/W_0\} \times 100 \quad \text{.....(4.2)}$$

Where Wt is the weight of tablet at time t and W_0 is the initial weight of tablet. The swelling will be calculated and then graph will be plot.

2.8.7 Dissolution Studies

The release rate of Cilnidipine from bio-adhesive matrix tablets will be determined using USP Dissolution Testing Apparatus II (Paddle type). The dissolution test will be performed using 900 ml 0.1 N HCL, at 37±0.5°C and 50 rpm. Aliquot volume will be withdrawn from the dissolution apparatus at specified time point, and the samples will be replaced with fresh dissolution medium. After filtration and suitable dilution the amount of drug release will be determined from the calibration curve.

Details of Dissolution Test:

1. Apparatus : USP Type II
2. Volume of medium : 900 ml
3. Temperature : 37 ˚C
4. Paddle Speed : 50 rpm
5. Dissolution medium used : 0.1 N HCL
6. Aliquot taken at each time interval: 5 ml

2.8.8 Bio-adhesive strength of the optimize formulation

The force required to separate the sample disk from model substrate were measured using a modified balance method. The formulation was fixed to the one side of the balance and come into contact with mucosal membrane of sheep or goat stomach, the tablets were left for 5 min for hydrate. A beaker was place on a moving platform. The beaker was then slowly raised until the substrate come in the contact with the formulation. On the other side of the balance fractional weight was added at a constant rate. The addition was stopped as soon as the detachment of formulation from the surface of mucosal membrane was obtained. The weights required for complete detachment was measured and expressed as bio-adhesive strength. Procedure was repeated for three more time for formulation. Average was recorded.

Calculation of the force of adhesion from the bio-adhesive strength.

Force of adhesion (F) = [W x g] / 1000 .....(4.3)

Where,

F = Force of adhesion in N
W = Bioadhesive strength in g
g = Acceleration due to gravity

III. RESULTS AND DISCUSSION

The present study was under taken to formulate cilnidipine sustained release tablet. The study involve pre-formulation of drug and excipients, formulation and development along with evaluation of tablet made with optimized formulation.

3.1 Identification of Drug

3.1.1 Melting Point Study

The cilnidipine was start melting at the temp 107^{0}c so observed melting point is in between 105^{0}c to 110^{0}c. The DSC test was done on Cilnidipine was presented below

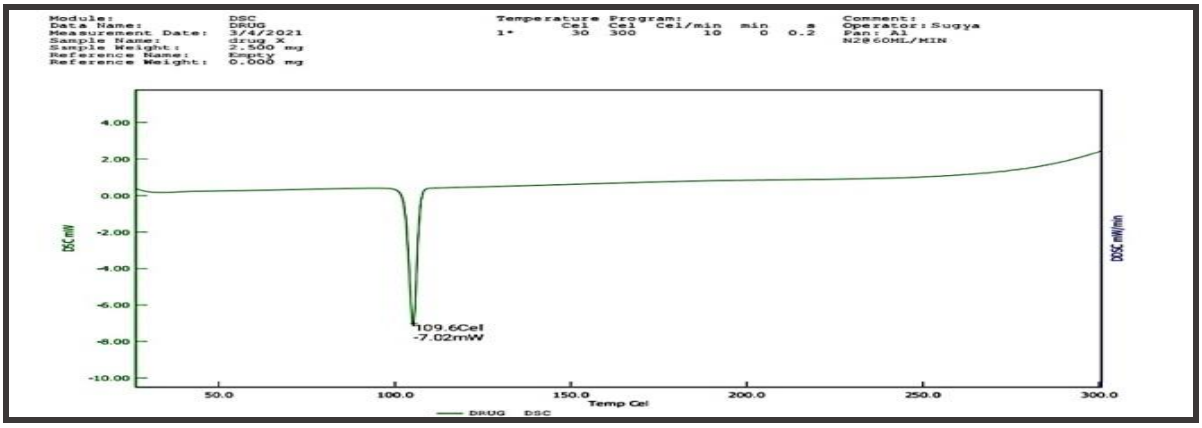

Figure 3.1: DSC graph of pure Drug

3.1.2 FTIR Absorption Spectroscopy Study

The IR spectrum of Cilnidipine was obtained by dispersing Cilnidipine in KBR disc. Major bends were obtained below in the table.

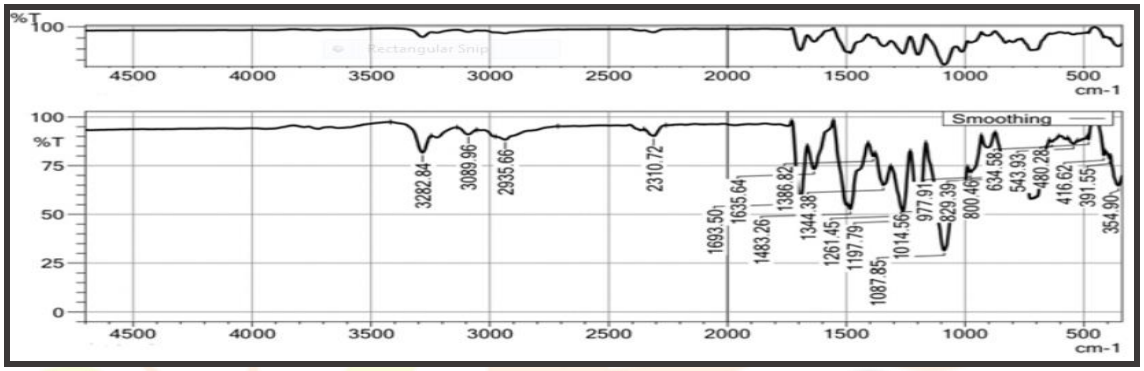

Figure 3.2: IR graph of pure drug

Table 3.1: Assignment of functional groups

Energy (cm^{-1})	Assignment
3282.8	N - H Stretching
1261.45	N = O Stretching
1344.38	N - O Stretching
2935.66	- OCH_3 Methoxy Stretching

From the value assigned in the table, super-imposition of spectra on the standard spectra of Cilnidipine as shown in the above graph and DSC, I concluded that the supplied API was identified as Cilnidipine.

3.1.3 Spectrometric Analysis Of Cilnidipine

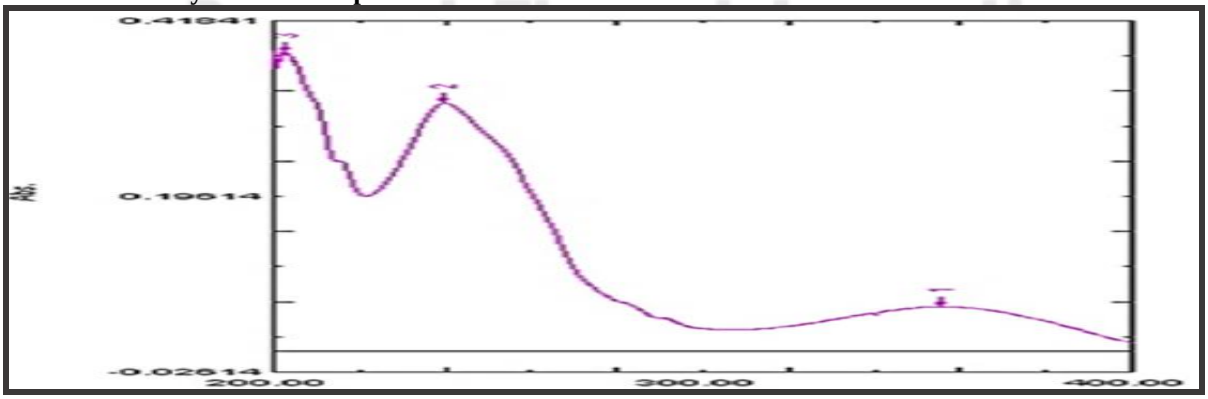

Figure 3.3: UV spectrum of Cilnidipine

Solution of Cilnidipine in methanol was scanned at 200 nm to 400 nm, one maxima is observed at 240 nm as shown in above Fig. This was confirmed with reported UV spectrum of Cilnidipine.

3.1.4 Preparation of Standard Calibration Curve

Table 3.2: Standard calibration curve of Cilnidipine in 6.8 phosphate buffer

Sr. No	Concentration µg/ml	Absorbance
0	0	0
1	2	0.038
2	4	0.077
3	6	0.115
4	8	0.16
5	10	0.208

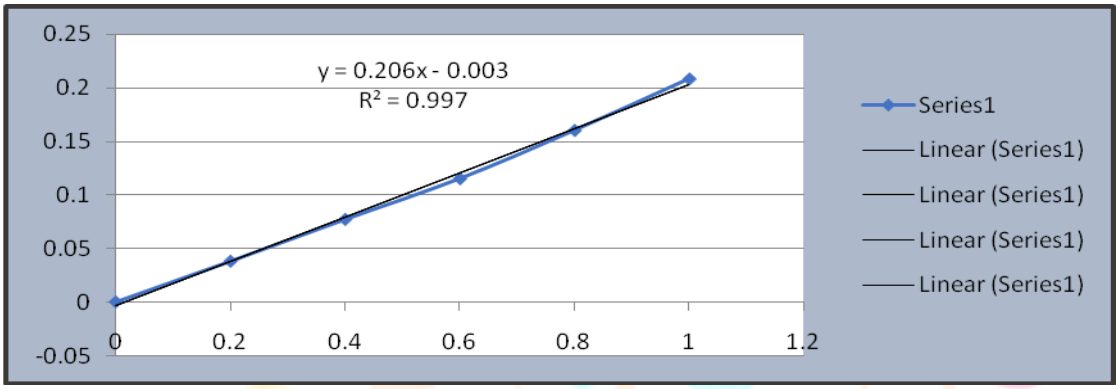

Figure 3.4: Standard calibration curve of Cilnidipine in 6.8 phosphate buffer

3.1.5 Solubility Study

Table 3.3: Solubility data of Cilnidipine

Medium	Solubility (mg/50ml)
Distilled Water	247
1.2 pH buffer	192
3.0 pH buffer	224
6.8 pH buffer	239
7.4 pH buffer	261

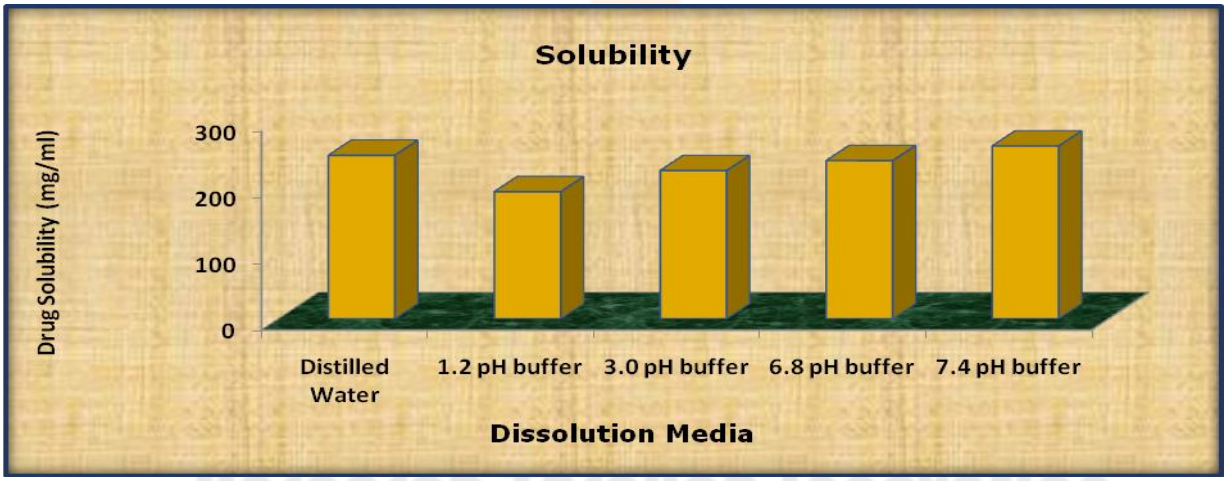

Figure 3.5: Solubility data of Cilnidipine

3.2 Micromeritics study evaluation

Table 3.4: Micromeritics study

Parameters of Flow Property of Cilnidipine				
Angle of Repose (θ)	**Bulk Density gm/cm³**	**Tapped Density gm/cm³**	**Hausners Ratio (H_R)**	**Compressibility Index(%)**
29.65	0.35	0.41	1.17	14.63

3.3 Calculation of % Yield of different Natural gum

Table 3.5: % Yield of different Natural gum

Natural Gum	% Yield
Sersuan	**32**
Rohen	**38**

Kekat	**27**
Sahaj	**39**
Albujia	**26**
Char	**31**
Tal	**29**

Figure 3.6: Prepared gum

3.4 Post-compression Evaluation of Natural Gum Tablets

Table 3.6: Post-compression Evaluation of Natural Gum Tablets

Parameters	Tablets containing Natural gum						
	Sersuan	**Rohen**	**Kekat**	**Sahaj**	**Albujia**	**Char**	**Tal**
Wt. variation	196-202	199-203	198-204	198-203	196-204	197-203	199-205
Hardness	4.9	4.5	5.2	5.1	5.0	4.6	4.7

3.5 Determination of Bio-adhesive strength of the Natural Gum Tablets

The force required to separate the sample disk from model substrate were measured using a modified balance method. The formulation was fixed to the one side of the balance and come into contact with mucosal membrane of sheep or goat stomach, the tablets were left for 5 min for hydrate. A beaker was place on a moving platform. The beaker was then slowly raised until the substrate come in the contact with the formulation. On the other side of the balance fractional weight was added at a constant rate. The addition was stopped as soon as the detachment of formulation from the surface of mucosal membrane was obtained.

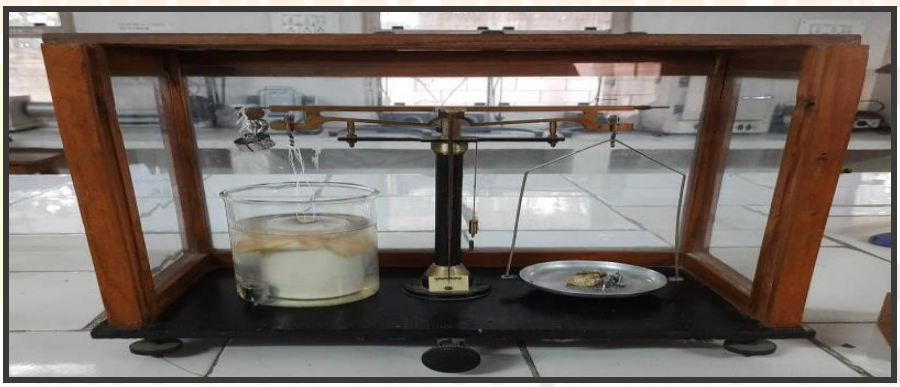

Figure 3.7: Modified balance during test

Table 3.7: Bio-adhesive Strength of Different Natural Gum

Natural Gum Tablets	Bio-adhesive strength (gm)	Force of adhesion (N/cm^2)
Sersuan	20.3	0.1993
Rohen	8.2	0.0805
Kekat	**28.5**	**0.2790**
Sahaj	5.2	0.0510
Albujia	27.5	0.2700
Char	15.8	0.1551
Tal	18.4	0.1806

From the above test it was concluded that *Acacia Karoo* (Kekat) have the better Bio- adhesive strength than the other gum, so we choose this gum to use in Preparation of Sustained Release Tablets of Cilnidipine.

3.6 Acute Oral toxicity study of the optimise gum *Acacia Karoo* (Kekat)

Wellness parameters observations of the treated as well as the control animals at 2,000 mg/kg body wt of *Terminaliaelliptica*dispersion

Table 3.8: Acute Oral toxicity study

Wellness parameter	30mi		4 hour		1day		2 days		7 days		14days	
	C	TE	C	TE	C	TE	C	TE	C	TE	C	TE
Skin fur	N	N	N	N	N	N	N	N	N	N	N	N
Alertness	N	N	N	N	N	N	N	N	N	N	N	N
Grooming	A	A	A	A	A	A	A	A	A	A	A	A
Torch response	N	N	N	N	N	N	N	N	N	N	N	N
Pain	N	N	N	N	N	N	N	N	N	N	N	N
Tremors	A	A	A	A	A	A	A	A	A	A	A	A
Gripping strength	N	N	N	N	N	N	N	N	N	N	N	N
Pinna reflex	N	N	N	N	N	N	N	N	N	N	N	N
Corneal reflex	N	N	N	N	N	N	N	N	N	N	N	N
Pupils	N	N	N	N	N	N	N	N	N	N	N	N
Salivation	N	N	N	N	N	N	N	N	N	N	N	N
Urination	N	N	N	N	N	N	N	N	N	N	N	N
Skin color	N	N	N	N	N	N	N	N	N	N	N	N
Lacrimation	N	N	N	N	N	N	N	N	N	N	N	N
Hyper activity	A	A	A	A	A	A	A	A	A	A	A	A
Mortality	A	A	A	A	A	A	A	A	A	A	A	A
Sleep	N	N	N	N	N	N	N	N	N	N	N	N

C-Control (Normal Saline), N-Normal, A-Absent, TE-Terminaliaelliptica dispersion in distilled water.

3.7 Method of Preparation of Sustained Release Tablets of Cilnidipine

Table 3.9: Determination of flow property

Ingredient	Parameters of Flow Property				
	Angle of Repose (θ)	Bulk Density gm/cm^3	Tapped Density gm/cm^3	Hausners Ratio (H_R)	Compressibility Index(%)
Cilnidipine	29.65	0.35	0.41	1.17	14.63
MCC-102	21.02	0.42	0.48	1.14	12.5
Gum	34.22	0.37	0.43	1.16	13.95
Mag. streate	29	0.44	0.51	1.15	13.72
Talc	30.45	0.35	0.42	1.2	16.66
Aerosil	26.27	0.57	0.64	1.12	10.93
$NaHCO_3$	33	0.67	0.76	1.13	11.84

Figure 3.7: Cilnidipine bio-adhesive sustained release tablets

3.8 Post-compression Evaluation of bio-adhesive sustained release tablets

Table 3.10: Post-compression Evaluation of bio-adhesive sustained release tablets

FR NO.	Hardness (Kg/cm^2)	Thickness (mm)	Friability %	Weight variation (mg)	Content uniformity %
CLN 1	4.5	3.72	0.32	197-202	98.8
CLN 2	5.2	3.45	0.48	198-204	98.1
CLN 3	4.6	3.35	0.15	199-205	99.2
CLN 4	4.8	3.49	0.19	196-202	96.6
CLN 5	5.1	3.60	0.30	195-201	93.9

3.9 Percentage Swelling Study

Table 3.11: Percentage Swelling Study

% Swelling study					
Time (hr)	CLN 1	CLN 2	CLN 3	CLN 4	CLN 5
0	0	0	0	0	0
2	16	19	21	25	29
4	19	23	29	34	37
8	24	27	36	42	44
16	29	31	42	49	51
24	32	39	49	54	57

All the tablets have different hydration profiles, as they hydrated gradually and swells more as the conc. of gum increases, reaching a maximum point after 24 hr. Most of the tablet reached between 16 to 29 % hydration with the first two hour. The fastest hydration rate was obtained from Batch CLN 5 that hydrated above 57 % within 24 hour.

3.10 Dissolution Test

The sample withdrawn was analysis using UV Spectrophotometer and maximum absorbance was taken at 240 nm. All the result are tabulated in the given below table.

In-Vitro Drug Release:

Release of drug from the Sustained Release matrix tablets varied according to the amount of Hydrophilic and Hydrophobic polymers

Table 3.12: Cumulative Drug Release

Time Hr	% Cumulative Drug Release				
	CLN 1	CLN 2	CLN 3	CLN 4	CLN 5
0	0	0	0	0	0
1	50.3	41.8	31.6	29.4	19.6
2	71.9	60.4	44.5	43.7	33.5
6	89.3	77.9	69.2	62.9	64.64
8	96.7	82.5	78.5	77.9	74.6
12	99.2	94.9	89.6	89.2	869
18	99.9	99.8	98.2	98.3	97.4
24	99.9	99.9	99.2	99.8	99.5

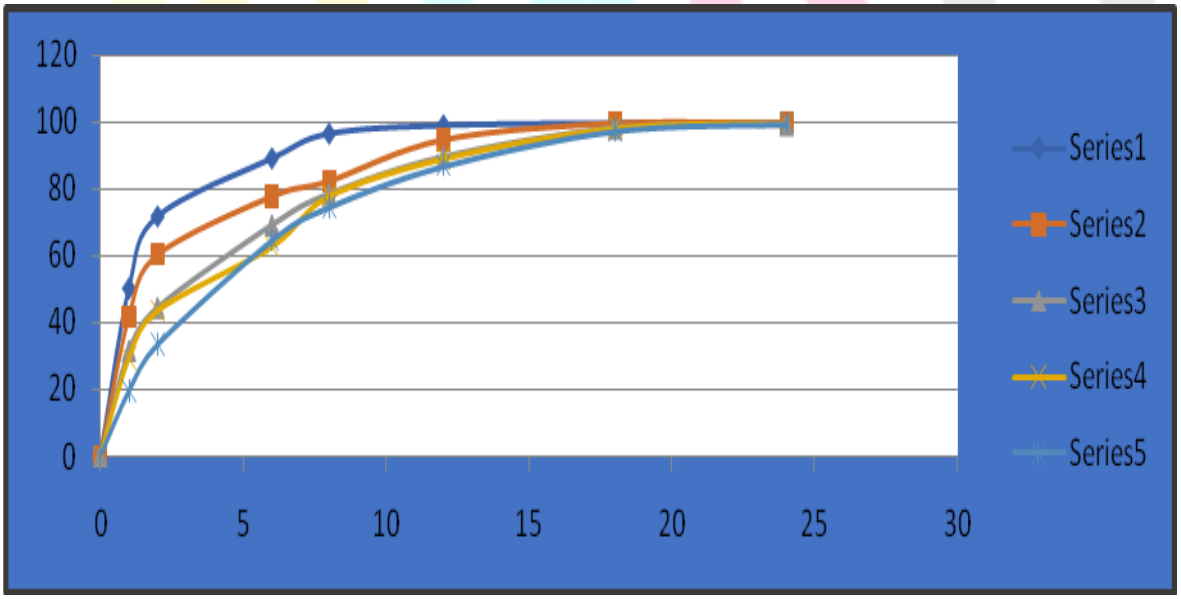

Figure 3.8: In vitro drug release from batch CLN 1- CLN 5

3.11 Bio-adhesive strength of the optimize formulation

Table 3.13: Bio-adhesive strength

Batch Code	Bio-adhesive strength (mg)
CLN 5	27.2

3.11.1 Calculation of The Force of adhesion (F) from the bio-adhesive strength

Force of adhesion (F) = [W x g] / 1000
= [27.2 X 9.82]/1000
= 0.267104 N
1 Newton = 100000 Dynes
So, 0.267104 N = 0. 267104 x 100000 = 26,710.4 Dynes/cm^2

IV SUMMARY AND CONCLUSION

Recent advances in novel drug delivery systems aim to enhance safety and efficacy of drug molecules by formulating a convenient dosage form for administration and to achieve better patient compliance. Once daily dosing of drugs having short elimination half life, through design of modified release oral formulation is the most preferred approach in improving patient convenience, drug therapy and safety. In the present investigation, an attempt was made to formulate a bio-adhesive sustained release matrix tablet formulation containing drug cilnidipine by using bio-adhesive natural gum.

Cilnidipine is a Calcium channel antagonist drug used in the treatment of hypertension in doses ranging from 05 mg to 20 mg. It is a slightly water soluble drug plasma half-life 2.1-2.5 hours. Hence, conventional tablet is insufficient to achieve the therapeutic plasma concentration for long duration of time and a dosage regime of twice or thrice daily is required.

The present study was aimed at designing a bio-adhesive sustained-release solid oral matrix tablet formulation of Cilnidipine through incorporation of swellable, soluble and erodible hydrophilic natural gum *Acacia Karoo* (Kekat) which bio-adhesive strength .

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