IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Design and Evaluation of a Biodegradable Mucoadhesive Drug Delivery System for Carvedilol: A Novel Approach to Sustained Cardio protection

1Dr. V. Leela Lakshmi*, 2Dr. M.Srinivasulu reddy,

3K. Praneeth, 4K. Sudeepthi, 5M. Dhana Lakshmi,

6I. Jeswika, 7B. Sravan Kumar

Department of Pharmaceutics, Narayana Pharmacy College, Chintha Reddy Palem, SPSR Nellore- 524002,

Andhra Pradesh .

ABSTRACT:

For creating mucoadhesive Carvedilol tablets, the current study used the mucilage of Ocimum basilicum seeds as a natural polymer in combination blends for long-lasting oral drug administration. Non-selective β-blockers having α1-blocking action, such as carvingilol, are frequently used to treat heart failure and hypertension. However, the drug's oral bioavailability is poor due to its short half-life, limited water solubility, and substantial first-pass metabolism. Therefore, it is preferable to use sustained release mucoadhesive formulations in order to increase therapeutic efficacy, decrease dosage frequency, and extend drug action. Ocimum basilicum L., a common medicinal herb. Its seeds contain a lot of mucilage, which can be used as a natural excipient in drug delivery systems because of its swelling, gel-forming, and mucoadhesive qualities.

The study's objectives were to separate and describe the mucilage found in O. basilicum seeds and use this natural polymer to create sustained-release mucoadhesive Carvedilol tablets. Determining the drug concentration, assessing the physicochemical characteristics of formulations, and researching in vitro drug release profiles over a 12-hour period were the specific goals.

An acetone–water (1:1) system was used to extract the mucilage from basil seeds, and FTIR and DSC methods were used to describe the results. Carvedilol sustained release tablets were made by direct compression with polymeric mixes containing varying amounts of basil mucilage. To ascertain flow characteristics, pre-compression parameters such as Hausner's ratio, Carr's Index, bulk density, tapped density, and angle of repose were measured. Hardness, friability, drug content, and weight variation were all examined after compression. Carvedilol's drug content was examined at 270 nm using UV-visible spectrophotometry. Drug release experiments were carried out in vitro in dissolving media for up to 12 hours.

Flow property analysis showed all formulations had acceptable ranges for angle of repose, Carr's Index, and Hausner's ratio. After 12 hours, the percentage drug release was: 92.3%, 90.3%, 93.4%, 91.3%, 97.2%, 85.2%, 89.8%, 89.4%, and 87.9% for different polymer ratios. The formulation containing 5% basil mucilage with 5% synthetic polymer achieved the highest release (97.2%).

The study demonstrated that Ocimum basilicum seed mucilage can be effectively utilized as a natural mucoadhesive polymer in the formulation of Carvedilol sustained release tablets. All formulations exhibited satisfactory physicochemical and mechanical properties with controlled drug release up to 12 hours. The 5% + 5% blend showed optimal release, indicating that basil seed mucilage is a promising, cost-effective, biocompatible excipient for sustained release drug delivery systems.

KEY WORDS: Carvedilol; Ocimum basilicum; Basil seed mucilage; Mucoadhesive tablets;

INTRODUCTION:

Because they are readily available locally, environmentally beneficial, and less expensive than imported synthetic items, plant products are used as a substitute for synthetic ones. With almost 10% of the global biodiversity wealth, India is one of the twelve mega biodiversity hubs. Pharmaceutical dosage forms such as tablets, syrups, suspensions, emulsions, ointments, and prolonged drug release systems are prepared using a variety of natural materials, including plant exudates, gums, mucilage, and starches. Because of their small size and effective carrier properties, microsphere microparticles are a significant component of this particulate DDS. When compared to traditional dosage forms, these delivery methods have several benefits, such as increased therapeutic efficacy of a particular medication and enhanced efficacy. Delivering the substance to the target tissue in the ideal quantity at the ideal time with low toxicity and adverse effects is essential for achieving optimal therapeutic efficacy.

Additionally, mucilage's are employed in medications for their ability to bind, thicken, stabilize, humidify, disintegrate, and control release. In both traditional and modern medicine, Ocimum basilicum is prized for its therapeutic and fragrant qualities. Ocimum contains aromatic herbs, shrubs, and shrubs of different fragrance compounds, all of which are quite valuable in the modern perfumery, food processing, and pharmaceutical industries. Asthma, inflammations, enlarged spleens, heart, brain, and blood disorders, as well as stomachic, stimulant, carminative, antipyretic, diaphoretic, expectorant, and diuretic properties, are all exhibited by the plant O. basilicum. Both individual and community health can benefit greatly from medicinal plants. Certain plants have therapeutic benefits because they contain chemical compounds that cause specific physiological reactions in the human body.

Alkaloids, phenolic compounds, flavonoids, and tannins are a few of these physiologically active components. Techniques for extraction and characterisation can be used to identify the bioactive components of medicinal plants. A constant quest for strong antibacterial agents has resulted from the characterization and understanding of the active ingredients, which can also help further examine the mode of action of the plant extracts generating the therapeutic effect. Some plant natural products have been used by humans as medicines, stimulants, and poisons. It is thought that natural products are essential to the physiology and ecology of the plants that produce them, especially as defense mechanisms against pests and diseases or as attractants for beneficial organisms like insect biological activities.

One of organic chemistry's main focuses is the clarification of their structures, chemistry, synthesis, and biosynthesis. The physiologically active components of commercial, therapeutic, and toxic plants have been investigated throughout organic chemistry's evolution. A significant number of these substances are secondary metabolites. There are other bioactive compound screening programs that have produced novel medications, such as Taxol, which is used to treat a variety of malignancies. Natural products frequently play an ecological function in controlling how insects, animals, microbes, and plants interact. They may be pheromones, attractants, defensive chemicals, or antifeedants. Drugs derived from medicinal plants have the advantages of being easy to use, efficient, and having a wide range of activity.

The WHO and several developing nations have rekindled interest in the value and application ofAfrican medicinal plants, which has prompted increased attempts to compile ethnomedical data related to medicinal endeavours. The reason for this is that most traditional healers do not maintain records, and they primarily transmit their knowledge orally from one generation to the next. In an effort to find new possibilities for creating better medications to treat microbial and viral diseases as well as cancer, researchers are focusing more and more on natural goods. The mints are a family of flowering plants that are classified as either Lamiaceae or Labiatae. Phylogenetic research, however, in the 1990s revealed that several genera classified under the Verbenaceae family actually belong in the Lamiaceae.

Sweet basil now holds the following taxonomic position according to the international code of botanical nomenclature: Kingdom: Plantae, Domain: Eukaryota, Botanical name: Ocimum basilicum; phylum: Tracheophyte; class: Magnoliopsida; order: Lamiales; family: Labiatae; genus: Ocimum. Along with a number of similar species or species hybrids that are also referred to as basil, O. basilicum comes in a wide variety. While

Thai basil (O. basilicum var. thyrsi flora), lemon basil (O. citriodorum), and holy basil (O. tenuiflorum) are used in Asia, the kind used in Italian cuisine is usually referred to as sweet basil. A cultivar called 'African Blue' and holy basil are two examples of basil that are perennial in warm, tropical conditions, however the majority of common kinds are considered annuals.

India and other tropical parts of Asia are the original home of basil, which has been grown there for over 5,000 years. The herb is primarily used in cooking. Numerous external environmental elements, such as temperature, soil type, geographic location, and even the amount of rainfall received by the individual plant, greatly influence the flavour and character of any given variety of basil. Pinene, camphene, ß-pinene, myrcene, limonene, cis-ocimene, camphor, linalool, methyl chavicol, y-terpineol, citronellol, geraniol, methyl cinnamate, eugenol, and other terpenes are among the chemical components found in basil extract.

The most often used polymers in solid dispersion formulation are poly (vinylpyrrolidone) (PVP) and poly (vinylpyrrolidone-co-vinyl acetate) (PVPVA), as well as cellulose derivatives like hydroxypropyl methylcellulose acetate succinate (HPMCAS) and vinyl hydroxypropyl methylcellulose (HPMC). These polymers should be able to sustain the supersaturated drug concentration in vivo. The use of plant-based polymers in various pharmacological dosage forms has been investigated. In different dosage forms, they have been used as binders, suspending agents, gelling agents, disintegrants, emulsifiers, binders, and bio adhesives. A

member of the allyl alkoxy-benzenes family of compounds, which also includes isoeugenol, eugenol, estragole, and safrole, is methyl eugenol [1,2-dimethoxy-4-(2-propenyl) benzene, which is present in sweet basil.

All these compounds typically enter the diet 'via a variety of different food sources, including spices (nutmeg, all spices), herbs (basil, tarragon), bananas and oranges. Many of these compounds are also found as components of natural oils used in perfume. Now a day's multi

drug resistance has developed due to the uncritical use of commercial antimicrobial drugs commonly used in the treatment of infectious disease. Antibiotics are sometimes associated with adverse effects on the host including hypersensitivity, immune-suppression and allergic reactions. Given the alarming incidence of antibiotic resistance in bacteria of medical importance, there is a constant need for new and effective therapeutic agents. Therefore, there is a need to develop alternative antimicrobial drugs for the treatment of infectious diseases from medicinal plants.

MORPHOLOGY AND PHYSICAL CHARACTERISATION OF BASIL SEEDS:

Table No.1: Physical properties of Basil seed:

Origin	Length(mm)	Width(mm)	Thickness(mm)	Species
Iran	**3.11**	**1.82**	**1.34**	**O. basilicum**
Iraq	**3.22**	**1.84**	**1.37**	**O. basilicum**
Serbia	**2.31-2.64**	**1.30-1.54**	**0.99-1.14**	**O. basilicum**
India	**1.97**	**1.06**	**ND**	**O. basilicum**

BENEFITS OF BASIL SEEDS:

Aids in weight loss:

Sabja seeds' high alpha-linolenic acid concentration makes them well-known for their ability to help people lose weight. Because of their high fiber content, they help you lose weight, avoid unpleasant cravings, and feel full for a long period.

Controls blood sugar levels:

It modulates the transformation of carbohydrates to glucose and slows down the body's metabolism. Even those with type 2 diabetes are advised to use it.

Relieve constipation and bloating:

Sabja seeds help to naturally cleanse your body by supporting regular bowel motions. It contains a volatile oil that acts as a stomach cleansing and aids in the elimination of gas from the digestive tract.

Treat acidity and heartburn:

Sabja seeds lessen acidity and heartburn by counteracting the body's reaction to HCL's acidic effects. Since we eat the seeds after they have been soaked in water, the water content calms the lining of the stomach and eliminates the burning sensation.

Good for skin and hair:

By mixing crushed Sabja seeds with coconut oil and applying it to the afflicted area, we can obtain the skinbene fitting properties of Sabja seeds.This aids in the treatment of psoriasis and eczema.Because sabja seeds are abun dant in iron, vitamin K, and proteinall of which are necessary for strong, long haithey have been shown to be go od for hair health.Because they contain antioxidants, they are also beneficial for the skin and hair.

Cure cough and cold:

One of the best natural stress relievers is Sabja seeds. As said earlier, they provide wonderful calming effects on our bodies that are somewhat similar to aromatherapy. Therefore, include these seeds in your regular diet results in less stress, improved mood, and increased mental Vigor and clarity.

Side effects of basil seed:

Some individuals may have symptoms such as diarrhoea, vomiting, nausea, acne, acid reflux, headache, abdominal discomfort, and loss of appetite after consuming basil seeds.

CARVEDILOL

DEFINITION OF CARVEDILOL:

The meaning of CARVEDILOL is a beta-blocker $C_{24}H_{26}N_2O_4$ that possesses some alpha-adrenergic blocking activity and is used to treat congestive heart failure. A synthetic antihypertensive methoxy phenoxy-2-propanol derivative with no intrinsic sympathomimetic activity, Carvedilol acts as a nonselective beta-adrenoceptor blocking agent (S (-) enantiomer) and as an alpha 1-adrenoceptor blocker (R (+) and S (-) enantiomers). Its acts more strongly on beta-receptors than on alpha 1-receptors, reduces peripheral vascular resistance by vasodilation, and prevents reflex tachycardia (beta-blockade) so that heart rate is either unchanged or decreased. Carvedilol also reduces renin release through beta-blockade.

PHYSICAL PROPERTIES:

White, round, or oval-shaped tablets with a film coating that contain 3.125 mg, 6.25 mg, 12.5 mg, or 25 mg of carvedilol are known as carvedilol. Carvedilol has a boiling point of 655.2 ± 0r-55.0°C at 760 mmHg.

PHARMACOKINETICS:

Because of its substantial first-pass metabolism, carvingilol is only about 25% to 35% accessible after oral dosing. Although food administration slows absorption, there is no discernible change in bioavailability. Orthostatic hypotension is less likely to occur when carvedilol is taken with food. 98 percent of carvedilol is attached to plasma proteins, primarily albumin. The steady-state volume of distribution of the basic, hydrophobic compound carvingilol is 115 L. The range of plasma clearance is 500–700 mL/min. Carvedilol is not believed to be peripherally selective because it is lipophilic and readily penetrates the blood–brain barrier in animals.

The chemical is broken down by the liver enzymes CYP2D6 and CYP2C9 by glucuronidation and aromatic ring oxidation, followed by glucuronidation and sulfation. Only a fraction of the parent compound's vasodilating effects is seen in the three active metabolites. But compared to the parent, the 4′-hydroxyphenyl metabolites have almost 13 times the β-blockade potency. After oral administration, carvedilol has an average elimination half-life of seven to ten hours. R (+)-carvedilol and S (-)-carvedilol, two enantiomorphs with different metabolic characteristics, are mixed together to form the medicinal product. Due to preferential selection for metabolism, the fractional half-life of R (+)-carvedilol is around 5 to 9 hours, while that of the S (–)-carvedilol fraction is 7 to 11 hours.

PHARMACODYNAMICS:

Carvedilol is both a non-selective β-adrenergic receptor antagonist (β_1, β_2) and an α-adrenergic receptor antagonist (α_1). The S (–) enantiomer accounts for the beta-blocking activity whereas the S (–) and R (+) enantiomers have alpha-blocking activity. The affinity (K_i) of carvedilol for the β-adrenergic receptors is 0.32 nm for the human β_1-adrenergic receptor and 0.13 to 0.40 nm for the β_2-adrenergic receptor using rat proteins, carvedilol has shown affinity for a variety of targets including:β_1-adrenergic receptor (K_i= 0.24–0.43 nm)β_2-adrenergic receptor (K_i= 0.19–0.25 nm)α_1-adrenergic receptor (K_i= 3.4 nm)α_2-adrenergic receptor (K_i= 2,168 nm)5-HT_1A receptor (K_i= 3,034 nm)D_2 receptor (K_i= 213 m)μ-opioid receptor (K_i= 2,700 nm)H_1 receptor (K_i= 207 nm)Veratridine site of voltage-gated sodium channels (IC_{50} = 1,260 nm)Norepinephrine transporter (K_i= 528 nm)Serotonin transporter (K_i= 627 nm)Dopamine transporter (K_i= 547 nm).

MECHANISM OF ACTION:

By blocking beta adrenoceptors, carvingilol prevents tachycardia brought on by exercise. By relaxing smooth muscle in the vasculature, carvingilol's effect on alpha-1 adrenergic receptors lowers peripheral vascular resistance and blood pressure overall. Higher dosages also exhibit antioxidant action and calcium channel blockage. Carvedilol's antioxidant properties stop low-density lipoprotein from oxidizing and being absorbed into the coronary circulation.

USES OF CARVEDILOL:

Heart failure and excessive blood pressure are treated with carvingilol. Reducing hypertension can help avoid heart attacks, strokes, and renal issues.

Carvedilol functions by preventing your body's natural chemicals, such epinephrine, from acting on your heart and blood arteries.

SIDE EFFECTS OF CARVEDILOL:

Common side effects of carvedilol include:

- Fatigue
- Dizziness
- Nausea
- Cough
- Vomiting
- Runny nose
- High blood pressure (hypertension)
- Palpitations
- Insomnia
- Bronchospasm
- Depression

MATERIALS AND METHODS:

Materials:

CRV was provided ex gratis by Alembic Pvt. Ltd. (Vadodara), sodium alginate (Research Lab. Pvt. Ltd. Mumbai), and calcium chloride (Ca Cl) (Research Lab. Pvt. Ltd. Mumbai). The O. basilicum seeds were procured from Green Pharmacy, Pune. All other chemicals employed were of analytical grade.

Method:

- Weigh about 100g of basil seeds
- The seeds were taken in a 1000ml beaker containing 900ml distilled water
- Allow to boil for at least 4-5 hr with continuous stirring at 40-60c for sufficient release of mucilage in water.
- The solution was concentrated until it becomes half of its initial volume
- The concentrated solution was filtered through muslin cloth to separate the filtrate and cool at room temperature.
- Add equal amount of acetone to the mucilage with the rapid stirring
- The mucilage is collected through muslin cloth
- The obtain mucilage is dried in hot air oven at 45c
- The dried powder was passed through sieve no 22

Preparation of polymers:

Polymers are the giant molecules of chemistry. The small building-block molecules are called monomers.

Synthetic polymers are a mainstay of modern life, but nature also makes polymers; they are found in all living matter.

reparation of synthetic polymers:

A prevalent but erroneous notion is that useful polymers, made by slap-dash procedures applied to impure starting materials. This is far from the truth; actually, the monomers used in most large-scale polymerizations are among the purest known organic substances. Furthermore, to obtain uniform commercially useful products, extraordinary care must be used in controlling the polymerization reactions. The reasons are simple – namely, formation of a high-molecular-weight polymer requires a reaction that proceeds in very high yields, and purification of the product by distillation, crystallization, and so on, is difficult, if not impossible.

Standardization of mucilage and polymer:

Polymer have been used as a main tool to control the drug release rate from the formulations. Extensive applications of polymer in drug delivery have been realized because polymers offer unique properties which so far have not been attained by any other materials. It comprises polymers with large number of a wide range of molecular weights, varying chemical compositions, low toxicity, and high stability.

Formulation of Carvedilol Sustained Release Tablets:

INGREDIENTS (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Carvedilol	20	20	20	20	20	20	20	20	20
Guar gum	5 (2.5%)	10 (5%)	15 (7.5%)	5 (2.5%)	10 (5%)	15 (7.5%)	5 (2.5%)	10 (5%)	15 (7.5%)
Sabja polymer	5(2.5%)	5(2.5%)	5(2.5%)	10 (5%)	10 (5%)	10 (5%)	15(7.5%)	15(7.5%)	15(7.5%)
Sodium bicarbonate	132	127	122	127	122	117	122	117	112
Micro crystalline cellulose	30	30	30	30	30	30	30	30	30
Stearic acid	5%w/v Sol	5%w/v Sol	5%w/v Sol	5%w/v Sol	5%w/v Sol	5%w/v Sol	5%w/v Sol	5%w/v Sol	5%w/v Sol
Citric acid	4	4	4	4	4	4	4	4	4
Talc	4	4	4	4	4	4	4	4	4
Total weight	200	200	200	200	200	200	200	200	200

PREFORMULATION STUDIES:

Preformulation activities range from supporting discovery's identification of new active agents to characterizing physical properties necessary for the design of dosage form. Critical information provided during preformulation can enhance the rapid and successful introduction of new therapeutics entities for humans. It is the first step in the rational development of dosage form.

Objective:

The overall objective of preformulation testing is to generate information useful in developing the formulation which is stable and bioavailability. Further the use of preformulation parameters maximizes the chances in formulating an acceptable, safe, efficacious and stable product. For any drug substance to formulate into a dosage form, it is necessary to study the physicochemical properties of the bulk drug like physical appearance, solubility, bulk density, tapped density, compressibility, melting point, molecular weight, sieve analysis.

A.P.I CHARACTERISATION:

1. Physical appearance

2. Solubility

3. Determination of bulk density and tapped density

4. Compressibility index

5. Angle of repose

1. Physical appearance:

A small quantity of Carvedilol powder was taken in butter paper and viewed in well illuminated place. Finally, the colour, odour and texture were observed.

2. Solubility:

A semi-quantitative determination of the solubility was made by adding solvent in small incremental amount to a test tube containing fixed quantity of solute or vice versa. After each addition, the system vigorously shaken and examined visually for any undissolved solute particles.

3. **Determination of bulk density and tapped density**:

It refers to a measurement to describe packing of particles and also used to determine the amount of drug that occupies the volume in mg/ml before tapping and after tapping an accurately weighed quantity of the powder (W), was carefully poured into the graduated cylinder and the volume (V_0) was measured, then the graduated cylinder was closed with lid, set into the density determination apparatus. The density apparatus was set for 100 taps and after that, the volume (VF) was measured and continued operation till the two consecutive readings were equal.

The bulk density and tapped density were calculated using the following formula:

Bulk density = W / V_0

Tapped density = W / VF

Where,
W = weight of the powder,
V_0 = initial volume,
VF = final volume

4. Compressibility index:

Compressibility was calculated from the powder density using the following formula:

$$\% \textbf{ Compressibility} = \left[\frac{pt - p0}{pt}\right] \times 100$$

Where,
Pt = Tapped density and
P_0 = Bulk density

5. Angle of Repose:

Angle of repose is used to determine the flow properties of powders, pellets or granules. The method to find angle of repose is to pour the powder on a conical heap on a level, flat surface and measure the included angle with the horizontal.

PRE COMPRESSION STUDIES FOR GRANULES

The granules were subjected for the following studies:

- Bulk density
- Tapped density
- Carr's index
- Hausner's ratio

Bulk density and tapped density:

A quantity of 4 gms of granules from each formula was introduced into a 10 ml measuring cylinder. After the initial volume was observed, the cylinder was tapped continuously until no further change in volume was observed.

BD=Weight of the powder/Initial volume powder

TD=Weight of the powder/Tapped volume

Carr's index:
The compressibility of the granules was determined by Carr's compressibility index. It is indirectly related to the relative flow rate, cohesiveness, and particle size. It is a simple test to evaluate the bulk density and tapped density of a powder and the rate at which it is packed.

Carr's index (%) =TD−BD/TD×100

Hausner's ratio: The Hausner's ratio is a number that is correlated to the flowability of a powder or granular material. It is calculated by using the given formula.

Hausner's ratio=TD/BD

I.P limits:

Hausner's ratio	Carr's Index	Flow
1.00-1.11	5-15	Excellent
1.12-1.18	12-16	Good
1.19-1.25	18-21	Fair to passable
1.26-1.34	23-35	Poor
1.35-1.45	33-38	Very poor
1.46-1.59	> 40	Very poor
> 1.60	5-15	Excellent

POST COMPRESSION STUDIES:

Thickness:

Tablet thickness can be measured using digital vernier callipers. 3 tablets were taken and their thickness was measured and the average thickness for each was calculated.

Hardness:

It is the force required to break a tablet by compression in the radial direction, it is an important parameter in formulation of mouth dissolve tablets because excessive crushing strength significantly reduces the disintegration time. In the present study the crushing strength of the tablet was measured using Monsanto hardness tester. An average of three observations is reported.

Friability Test:

Friability of the tablets was determined using Roche friability. This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Pre-weighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed.

%Friability=Initial weight – Final weight/Initial weight×100

Weight variation:

The weight variation test is done by weighing 10 tablets individually, calculating average weight and comparing the individual tablet weights to the average. The tablets meet the USP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

%Weight variation=Average weight – Initial weight/Average weight×100

USP limits:

Average weight of tablets	Max. percentage difference
130 or less	10
130–324	7.5
More than 324	5

Drug content:

Five tablets were taken and powdered; the powder equivalent to 20 mg of Carvedilol was dissolved in 100 ml of 0.1 M HCl of pH 1.2, filtered and analysed at 350 nm using UV-Visible spectrophotometer.

In vitro dissolution studies:

Apparatus : USP APPARATUS – II

Medium : 0.1 N HCl up to 1st two hours, 6.8 pH Phosphate buffer for remaining 10 hours.

Sampling interval : 1st hr, 2nd hr, 4th hr, 6th hr, 8th hr, 10th hr & 12th hr

rpm : 100

Temperature : 37°C ± 0.5°C

Procedure:

Using the USP Type-II apparatus, in vitro dissolution tests of Carvedilol SR tablets were carried out. 900 ml of 0.1 M HCl at pH 1.2 was used as the dissolution medium for the first two hours of the dissolution investigations, which were conducted at 37±0.5°C and 100 rpm. For the final ten hours, 6.8 pH phosphate buffer was used in its place. Each formulation's tablet, which contained 20 mg of medication, was put into the dissolve media. Five millilitre aliquots of the sample were taken out at regular intervals. Each time, the identical amount of brand-new dissolving medium was used in lieu of the removed sample.

RESULT:

Preformulation study of Active Pharmaceutical Ingredient

S. No	Characteristics	Results
1.	Physical appearance	Brownish yellow
2.	solubility	Sparingly soluble in cold water
3.	Bulk density	0.732g/C
4.	Tap density	0.632g/C
5.	Compressibility index	12.75%
6.	Melting point	173oc(3430F)

Fourier-transform infrared spectroscopy (FTIR):

The FTIR spectrum of the O. basilicum mucilage was recorded on the FTIR (Alpha-E and Bruker) spectrophotometer. The base line correction was done by blank background measurement, and then the spectrum of dried mucilage was run. By running the IR spectra of drug and polymer, it will help in identifying the groups and also help in detecting if any interaction occurs between the reagent.

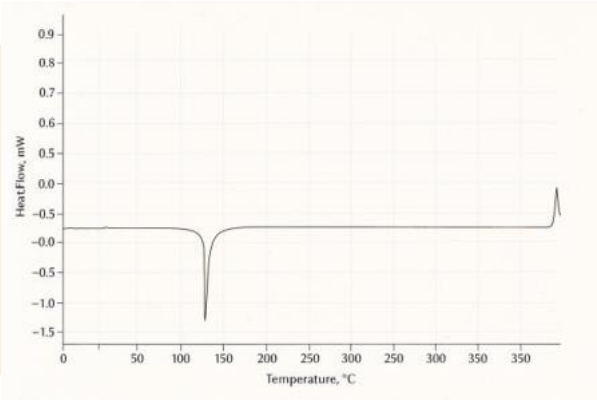

Figure1.FTIR spectrum of the O. basilicum mucilage

Differential scanning calorimetry analysis of mucilage:

Differential scanning calorimetry (DSC) was used to measure the occurrence of exothermal or endothermal changes with an increase in temperature. The DSC thermograms of IND, OBM, and solid dispersions are shown in figure 2.

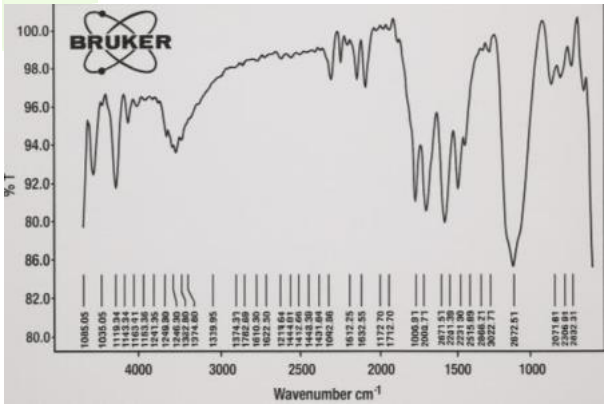

Figure 2. Differential scanning calorimetry analysis of mucilage

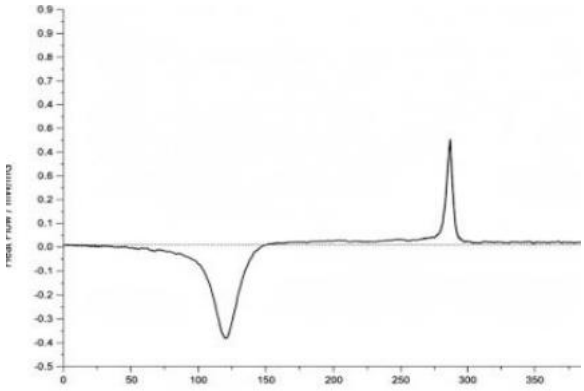

Figure 3. FTIR-Compatibility of carvedilol with natural Sabja polymer

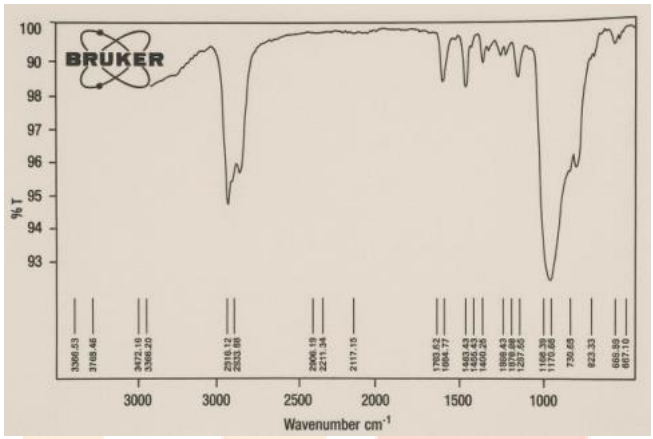

Figure 4.DSC-Compatibility study of carvedilol with Sabja polymer

In vitro dissolution rate study:

In vitro dissolution test studies were carried out by varying the dissolution medias to see its effect on percentile drug release. Following table 2 gives the results of effect of dissolution media on rate of drug release from solid dispersions. The results reflected that dissolution media affects the drug release pattern variably. It was observed that dissolution rate of SD's prepared by kneading method was increased significantly as compared to original drug in phosphate buffer pH 7.2(1 parts in phosphate buffer pH 7.2+4 parts DW as per Indian pharmacopoeia) dissolution media. The increase in dissolution rate was found to be 4-fold greater in physical mixture while in case of co- grinding method dissolution pattern was observed 1.7-fold greater. Solvent drop method increased the dissolution rate by 2.8-fold. Kneading method was found to give better drug release as compared to other methods since the dissolution rate was increased 7.2-fold. Pure drug didn't give any drug release in distilled water whereas the solid ~~dispersions gave significant increase in dissolution rate in distilled water. SD's prepared by kneading method gave highest drug release as compared~~ to other methods. The increase in dissolution rate of IND SDS in distilled water may be attributed to the hydrophilic nature of OBM which might have incorporated insoluble drug moiety into hydrophilic core thus facilitating its dissolution behaviour and maintaining drug in supersaturated level. The drug was found to be released and also the drug release was increased in all formulations by using phosphate buffer pH 6.8 as dissolution media.

CALIBRATION CURVE OF CARVEDILOL:

Table No.1: Standard curve data using 0.1M HCL of Ph 1.2

CONCENTRATION (mcg/ml)	Absorbance
5	0.152
10	0.308
15	0.453
20	0.624
25	0.760

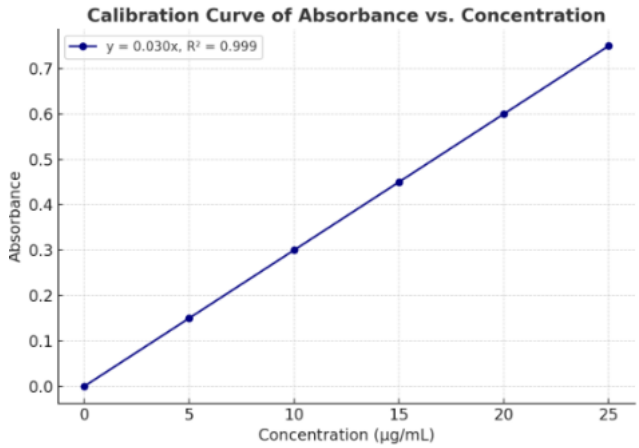

Figure 5. Standard curve by using above data

Table No.2: Standard curve data of carvedilol using pH 6.8 Phosphate Buffer

Concentration(mcg/ml)	Absorbance
5	0.126
10	0.252
15	0.378
20	0.508
25	0.634

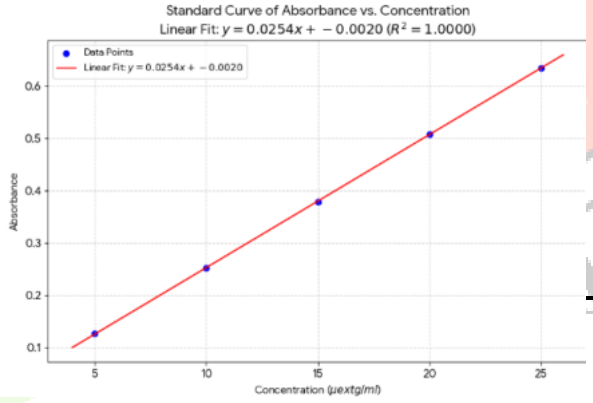

Figure 5. Standard Curve of carvedilol by using above data

PRECOMPRESSION STUDIES:

S.NO	FORMULATION CODE	ANGLE OF REPOSE	BULK DENSITY	TAPPED DENSITY	COMPRESSIBILITY INDEX	HAUSNERS RATIO
1	F1	29.51	0.71	0.84	15.45	1.181
2	F2	27.41	0.74	0.86	14.28	1.176
3	F3	27.32	0.73	0.85	14.11	1.196
4	F4	26.93	0.71	0.82	13.41	1.216
5	F5	28.14	0.72	0.85	15.29	1.193
6	F6	25.85	0.75	0.85	11.76	1.197
7	F7	26.06	0.79	0.87	16.47	1.216
8	F8	27.40	0.76	0.90	17.77	1.186
9	F9	28.68	0.74	0.87	16.01	1.193

The weight of tablets of all formulations was found to be in range of 198.16 to 201.10. Hardness test for all formulations was carried out and observations obtained were in the range of 7.5 to 10.5 kg/cm2. Hardness for all formulations was observed to be proper, which signify that crushing strength of all formulations was maintained after compression. The thickness of all formulations was found to be in the range of 3.11 to 3.84mm. Friability test was conducted for all formulations, % friability was found to be in range of 0.220 to 0.814.

POST COMPRESSION STUDIES:

Formulation code	Weight variation(mg)	Thickness(mm)	Hardness(kg/cm2)	%Friability
F1	198.26	3.32	7.52	0.318
F2	199.86	3.80	9.06	0.321
F3	199.42	3.76	10.32	0.834
F4	200.11	3.84	9.43	0.345
F5	200.59	3.75	9.03	0.511
F6	200.75	3.62	8.43	0.220
F7	200.96	3.71	10.01	0.814
F8	200.90	3.45	7.52	0.364
F9	201.10	3.11	7.88	0.501

The weight of tablets of all formulations was found to be in range of 198.16 to 201.10. Hardness test for all formulations was carried out and observations were obtained in the range of 7.5 to 10.5kg/cm2.Hardness for all formulations was observed to be proper, which signify that crushing strength of all formulations was maintained after compression. The thickness of all formulations was found to be in the range of 3.11 to 3.84 mm. Friability

test was conducted for all formulations, %friability was found to be in the range of 0.220 to 0.814.

DRUG CONTENT:

S.NO	Formulation code	Drug content
1	F1	97.66
2	F2	96.25
3	F3	98.33
4	F4	98.45
5	F5	99.86
6	F6	97.45
7	F7	101.05
8	F8	98.66
9	F9	96.98

Drug content of all formulations was observed between 96.25 to 101.05%. Drug content for all formulations was within the range which indicated that there were uniform flow and uniform distribution of drug

S. No	Time (hrs)	F1	F2	F3	F4	F5	F6	F7	F8	F9	INNOVATOR
1	1	23.80	22.80	18.14	19.21	**20.13**	21.29	22.70	23.67	19.85	21.53
2	2	32.26	32.20	37.40	38.36	**34.46**	36.85	38.15	37.10	38.23	36.14
3	4	54.50	55.61	55.12	57.67	**50.19**	55.26	56.74	54.63	55.76	52.76
4	6	62.14	64.27	59.17	60.23	**64.21**	64.36	69.85	70.55	62.92	66.22
5	8	71.87	73.54	70.24	72.69	**77.15**	80.52	74.35	70.68	72.95	80.59
6	10	80.49	82.21	83.69	81.58	**87.99**	79.14	80.68	84.66	85.73	89.95
7	12	92.30	90.3	93.4	91.3	**97.2**	85.2	89.8	89.4	87.9	98.64

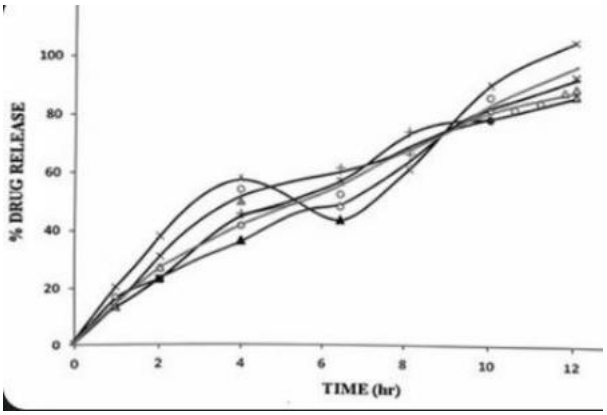

Figure 6. Dissolution profile of all carvedilol SR Tablets

In-vitro dissolution studies on all formulations had been conducted. The results were compared with that of the innovator product. From the above data it can be confirmed that formulation F5 was similar to the innovator product.

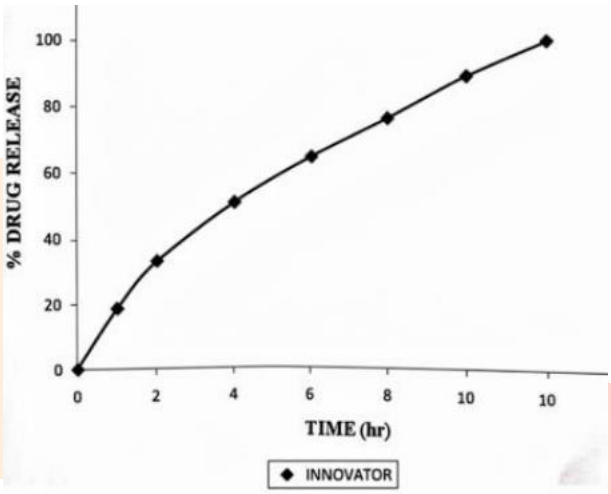

Figure 7. Dissolution Profile of Innovator

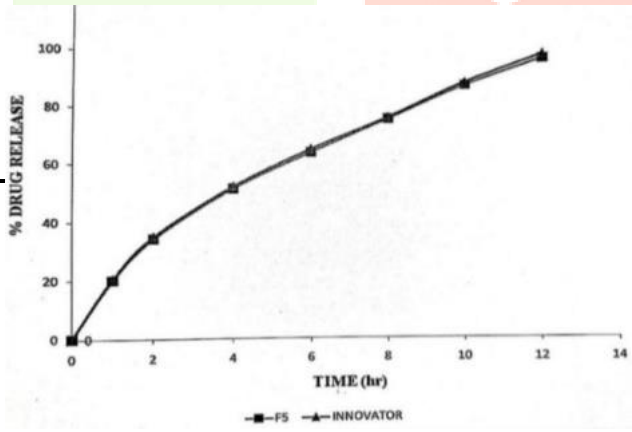

Figure 8. Dissolution Profile of Best Formulator(F5) &Innovator

CONCLUSION:

The mucilage isolated from these seeds of *O. basilicum* will be useful as an excipient for oral drug delivery systems as the results of phytochemical and physicochemical tests indicated the suitability of mucilage for tablet dosage form as well as a suspending agent for suspension due to its flowability, weakly acidic pH, swelling potential, and viscous in nature. The present study suggests that isolated mucilage from the seeds of *O. basilicum* showed good flow properties. All the studies hence showed that the mucilage obtained can act as a potentially good candidate for various pharmaceutical formulations for its high swell ability on coming in contact with water thus it can be used as a thickening agent, suspending agent or as a super disintegrant in various forms.

The percentage drug content of Carvedilol was determined by extraction with acetone and analysed by using UV-Visible Spectrophotometer at 270 nm. After 12th hour the percentage drug release from the formulations were 92.3%, 90.3%, 93.4%, 91.3%, 97.2%, 85.2%, 89.8%, 89.4%, 87.9% for the formulations containing sabja polymer 2.5%&2.5%, 5%&2.5%, 7.5%&2.5%, 2.5%&5%, 5%&5%, 7.5%&5%, 2.5%&7.5%, 5%&7.5% and 7.5%&7.5%

(Table 7) respectively. Formulation F5 was identified to be the best as it showed sustained action for 12 hr and as it matches well with the innovator (Table 5). Accordingly, it can be concluded that the F5 (5% w/w sabja polymer) is robust one.

CONFLICT OF INTEREST: The authors have no conflicts of interest regarding this investigation**.**

REFERENCES:

1. Kadam PV, Yadav KN, Jagdale SK, Shiva tare RS, Sumeet K, Patil MJ. Evaluation of *Ocimum sanctum* and *Ocimum basilicum* mucilage as a pharmaceutical excipient. *J Chem Pharm Res.* 2012;4(4):1950–1955.

2. Mishra S, Bhandari A, Parvez N, Sharma PK. Extraction and use of *Lallemantia royleana* seed. *J Chem Pharm Res.* 2015;4(4):1578–1589.

3. Bucktowar K, Bucktowar M, Bholoa LD. A review on sweet basil seeds (*Ocimum basilicum*). *J Pharm Res.* 2016;5(12):554–567.

4. Patwekar S, Barmade MK. Controlled release approach to novel multiarticulate drug delivery system. *Int J Pharm Sci.* 2012; 4:757–763.

5. Wong CY, Al-Salami H, Dass CR. Microparticles, microcapsules and microspheres: Areview of recent developments and prospects for oral delivery of insulin. *Int J Pharm.* 2018; 537:223–244.

6. Patel MM. Formulation and development of pH-dependent microparticulate system for colon-specific drug delivery. *Drug Deliv Transl Res.* 2017; 7:312–324.

7. Oliveira MB, da Silva JB, Montanha MC, Kimura E, Diniz A, Bruschi ML, et al. Design and characterization of mucoadhesive gelatin-ethylcellulose microparticles for the delivery of curcumin to the bladder. *Curr Drug Deliv.* 2018; 15:1112–1122.

8. Jani GK, Shah DP, Prajapati VD, Jain VC. Gums and mucilage's: versatile excipients for pharmaceutical formulations. *Asian J Pharm Sci.* 2009; 4:308–322.

9. Malviya R, Srivastava P, Kulkarni GT. Applications of mucilage in drug delivery: a review. *Adv Biol Res.* 2011; 5:1–7.

10. Bhasin M. *Ocimum*—taxonomy, medicinal potentialities and economic value of essential oil. *J Biosphere.* 2012; 1:48–50.

11. Bhowmik D, Chiranjib B, Chandira RM. Fast dissolving tablet: an overview. *J Chem Pharm Res.* 2009;1(1):163–177.

12. Vale A. Paracetamol (acetaminophen). *Medicine (Baltimore).* 2012;40(3):144–146.

13. Lino A, Deogracious O. The in vitro antibacterial activity of *Annona senegalensis*, *Securidacca longipendiculata* and *Steanotaenia araliacea*—Ugandan medicinal plants. *Afr Health Sci.* 2006; 6:31–35.

14. Ikwu DE. Evaluation of the chemical composition of indigenous spices and flavouring agents. *Glob J Pure Appl Sci.*

2001;7(3):455–459.

15. Harborne JB. *Phytochemical Methods: A Guide to Modern Techniques of Plant Analysis.* 2nd ed. New York: Chapman & Hall; 1998. p. 5–11.

16. Cseke LJ, Kirakosyan A, Kaufman PB, Duke JA, et al. *Natural Products from Plants.* 2nd ed. Boca Raton: CRC Press; 2006.

17. McCorkle CM. Back to the future: lessons from ethnoveterinary research, development and extension for studying and applying local knowledge. *Agric Food Hum Values Soc.* 1995; 22:52–80.

18. Tatyana V, Morales R, Krestovskaja J, Paton A, Ryding O. "Labiatae" pages. In: The Families and Genera of Vascular Plants. Vol VII. Berlin: Springer; 2004. p. 167–275.

19. Wagstaff SJ, Hickerson L, Spangler R, Reeves PA, et al. Phylogeny in *Labiatae L.*, inferred from cpDNA sequences. *Plant Syst Evol.* 1998; 209:265–274.

20. November E, Aerts R, Behailu M, Muys B. Species list Tigrinya–Scientific. *Technical Note* 2002/4. Forest Rehabilitation Project, Mekelle University, Ethiopia and K.U. Leuven, Belgium; 2002.

21. Chaudhari, P. G., et al. (2024/Recent). Formulation and Evaluation of Mucoadhesive Buccal Tablets of Carvedilol. *Journal of Drug Delivery and Therapeutics*, (Relevant Volume and Issue). (Focus on HPMC K4M and Xanthan Gum).

22. Khafagy, E-S., et al. (2022). Preparation and Characterization of a Novel Mucoadhesive Carvedilol Nanosponge: A Promising Platform for Buccal Anti-Hypertensive Delivery. *Gels*, 8(4), 235.

23. Reddy, K. G., et al. (2013). Formulation and Evaluation of Sustained Release Sodium Alginate Microbeads of Carvedilol. *Research Journal of Pharmacy and Technology*, 6(4), 570-575. (Uses Sodium Alginate, HPMC, Chitosan).

24. Hassan, K., et al. (2013). Mucoadhesive buccal patches based on interpolymer complexes of chitosan–pectin for delivery of carvedilol. *Archives of Pharmacal Research*, 36(4), 481–488.

25. Nayak, A. K., et al. (2024/Recent). Formulation and Evaluation of a Bilayer Mucoadhesive Buccal Drug Delivery System for Carvedilol Nanoparticles. *International Journal of Pharmaceutical Sciences*, 2(7), 2010-2018.

26. Kumria, R., et al. (2007). Mucoadhesive buccal patches of carvedilol: formulation and evaluation. *Indian Journal of Pharmaceutical Sciences*, 69(4), 524-528.

27. Patel, B. R., et al. (2018). Development of an Electrospun Patch Platform Technology for the Delivery of Carvedilol in the Oral Mucosa. *Nanomaterials*, 12(3), 438.

28. Garg, R., et al. (2015). Design and evaluation of mucoadhesive microparticles of carvedilol for nasal delivery. *Acta Pharmaceutica Sinica B*, 5(1), 22–31.

29. Ahuja, M., et al. (2016). Chitosan as Valuable Excipient for Oral and Topical Carvedilol Delivery Systems. *Molecules*, 14(8), 712.

30. Raju, Y. P., et al. (2014). Formulation and evaluation of Carvedilol melt in mouth tablet using mucoadhesive polymer and PEG-6 stearate as hydrophilic wax binder. *International Journal of Pharmacy*, 4(2), 1-7.

31. Chaves, P. S., et al. (2017). Carvedilol-loaded nanocapsules: Mucoadhesive properties and permeability across the sublingual mucosa. *International Journal of Pharmaceutics*, 518(1-2), 174-184.

32. Singh, B., et al. (2015). Optimization of mucoadhesive buccal tablets of carvedilol by 3^2 factorial design. *International Journal of Pharmaceutical Investigation*, 5(2), 114–120.

33. Reddy, M. S., et al. (2019). Mucoadhesive microspheres of carvedilol for enhanced bioavailability. *Journal of Advanced Pharmaceutical Technology & Research*, 10(4), 163-170.

34. Formulation and Evaluation of Mucoadhesive Chitosan Microspheres of Carvedilol for Nasal Administration. (2024/Recent). *IP International Journal of Comprehensive and Advanced Pharmacology*, 7(4), 3350.

35. Grabovac, V., et al. (2005). Comparison of the mucoadhesive properties of various polymers. *Advanced Drug Delivery Reviews*, 57(11), 1713–1723.

36. Khutoryanskiy, V. V. (2011). Advances in mucoadhesion and mucoadhesive polymers. *Macromolecular Bioscience*, 11(6), 748–764.

37. Ludwig, A. (2005). The use of mucoadhesive polymers in ocular drug delivery. *Advanced Drug Delivery Reviews*, 57(11), 1595–1639. (Applicable to other mucosal routes).

38. Bernkop-Schnürch, A., et al. (2004). Thiolated polymers—"thiomers": synthesis and pharmaceutical applications. *Advanced Drug Delivery Reviews*, 56(11), 1579–1587.

39. Veuillez, F., et al. (2001). Factors and strategies for improving buccal absorption of peptides. *European Journal of Pharmaceutics and Biopharmaceutics*, 51(2), 93-109. (General principles for buccal delivery).

40. Lehr, C. M., et al. (1992). In vitro evaluation of mucoadhesive properties of chitosan and some other natural polymers. *International Journal of Pharmaceutics*, 78(1-3), 43–48.

41. Carvalho, F. C., et al. (2010). Mucoadhesive drug delivery systems. *Brazilian Journal of Pharmaceutical Sciences*, 46(1), 1–18.

42. Kumar, K., et al. (2014). Bioadhesive polymers: novel tool for drug delivery. *Artificial Cells, Nanomedicine, and Biotechnology*, 42(4), 274–283.

43. Smart, J. D. (2005). The basics and underlying mechanisms of mucoadhesion. *Advanced Drug Delivery Reviews*, 57(11), 1556–1568.

44. Peppas, N. A., & Buri, P. A. (1985). Surface, interfacial and molecular aspects of polymer bioadhesion on soft tissues. *Journal of Controlled Release*, 2(4), 257–275.

45. Boddupalli, B. M., et al. (2010). Mucoadhesive drug delivery system: An overview. *Journal of Advanced Pharmaceutical Technology & Research*, 1(4), 381–387.

46. Sosnik, A., & Chilvers, G. R. (2016). Mucoadhesion: Polymer–mucus interactions and their impact on drug delivery systems. *Advanced Drug Delivery Reviews*, 96, 1–20.

47. Hägerström, H. (2003). Polymer gels as pharmaceutical dosage forms. *Acta Universitatis Upsaliensis*. (Comprehensive Thesis/Monograph on Mucoadhesive Gels).

48. Hansen, G. B., & Peppas, N. A. (2020). Synthesis and Characterization of Novel Stimuli-Responsive Copolymers for Oral Drug Delivery. *Macromolecules*, 53(1), 193–200. (Methodology and Polymer Synthesis).

49. Rathore, K. S., et al. (2017). Mucoadhesion and its applications in drug delivery: a comprehensive review. *International Journal of Pharma and Bio Sciences*, 8(2), 1-15.

50. Shukla, P. K., et al. (2010). Formulation and evaluation of mucoadhesive chitosan microspheres of carvedilol for nasal administration. *Journal of Drug Targeting*, 18(4), 321-331.