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FORMULATION AND EVALUATION OF HYDROPHOBIC POLYMER BASED MATRIX SUSTAINED RELEASE TABLETS OF CAPTOPRIL

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ABSTRACT
The purpose of the present study was to prepare oral sustained release matrix tablets of highly water soluble drug, Captopril using a hydrophobic polymer compritol (glyceryl behenate) and to evaluate the effect of hydrophobic polymer and effect of methods of preparation on the release of the drug The tablets were prepared by direct compression, wet granulation techniques. The matrix tablets were evaluated for various parameters as physical appearance, dimensions, hardness, weight variation, friability, drug content, in vitro dissolution studies. Also the matrix tablets prepared by hot melt granulation showed more effective retarded release rate than tablets prepared by direct compression and wet granulation techniques. Compritol 888 ATO can be used as a matrix former to sustain the release of water soluble drugs. Tizanidine hydrochloride tablets were prepared by melt direct compression technique using xanthum gum, glyceryl behenate, glyceryl monostearate and stearic acid in different proportion. Formulated sustend release tablets were evaluated for appearance, dimensions (diameter and thickness), weight varation, hardness, friability, drug content and in-vitro release of Tizanidine hydrochloride.

KEYWARD: Oral sustained release matrix tablets, Tizanidine hydrochloride, Hydrophobic polymer compritol, Matrix tablets, Compritol 888 ATO, Glyceryl behenate.

INTRODUCTION

ORAL DRUG DELIVERY SYSTEM

Oral drug delivery systems have required innovation in materials science to provide materials biocompatible with body tissues during prolonged contact. For cost and patient convenience, oral delivery certainly would be an attractive method. Besides, where delivery rate control is critical, oral delivery, even when possible, would probably be insufficiently precise. Oral delivery would also limit the substance to bloodstream delivery to the disease site.

While the oral route is the most convenient method of drug administration, advances in oral drug delivery technologies have been limited. One of the reasons for this is the limitations imposed by the unique GI physiology illustrated. In these areas, even small improvements in drug delivery technology can make significant differences in enhancing patient compliance and drug bioavailability. Ranade et al (2011)

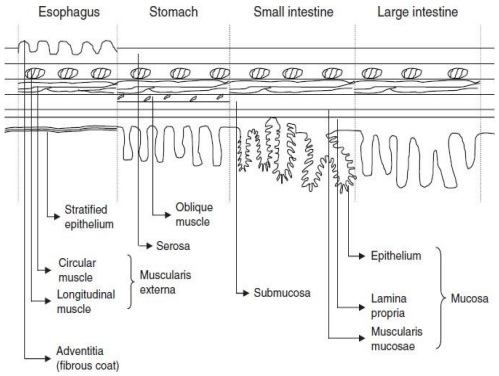

Fig 1.1: Layers of Gastrointestinal Tract. Xiaoling et al (2006)

The absorption, distribution, metabolism, and excretion of a drug all involve passage across cell membranes. Mechanisms by which drugs cross membranes and the physicochemical properties of molecules and membranes are critical to understand the disposition of drugs in the human body.

The characteristics of a drug that predict its movement and availability at site of action are its molecular size and shape, degree of ionization, relative lipid solubility of its ionized and unionized forms, and its binding to serum and tissue proteins. In most cases, a drug must traverse the plasma membranes of many cells to reach its site of action. Although barriers to drug movement may be a single layer of cells (intestinal epithelium) or several layers of cells and associated extracellular protein (skin), the plasma membrane represents the common barrier to drug distribution.

Region of the GI tract	Length, cm	Internal diameter, cm	Volume, mL	Surface area, cm^2	pH	Average residence time
Entire GI tract	530–870	3–9		2×10^5	1.5–7	Up to 38 h
Mouth cavity	15–20	10		700		
Esophagus	20	2–4		200		
Stomach						
Fasted state	25	15	25–50		1.4–2.1	0.5–1.5 h
Fed state			1000–1600		2–5	2–6 h
Small intestine	370–630	3–5		$2.1–5.9 \times 10^{6a}$	4.4–7.4	3 ± 1 h
Duodenum	20–30	3–5		113,000–283,000[a]	4.9–6.4	3–10 min
Jejunum	150–260	3–5		270,000–750,000[a]	4.4–6.4	0.5–2 h
Ileum	200–350	3–5		360,000–1,050,000[a]	6.5–7.4	0.5–2.5 h
Large intestine	150	3–9		15,000	5.5–7.4	Up to 27 h
Caecum	7	7		500	5.5–7	
Colon	90–150	3–9		15,000	7.4	
Rectum	11–16	2.5		150	7	

Fig. 1.2: Physical characteristics of gastrointestinal tract. Xiaoling et al (2006)

ORAL SUSTAINED DRUG DELIVERY SYSTEM

Pharmaceutical products designed for oral delivery are mainly immediate release type or conventional drug delivery systems, which are designed for immediate release of drug for rapid absorption. These immediate release dosage forms have some limitations such as-

a) Drugs with short half-life require frequent administration, which increases chances of missing dose of drug leading to poor patient compliance.
b) A typical peak-valley plasma concentration-time profile is obtained which makes attainment of steady state condition difficult.

d) The fluctuating drug levels may lead to precipitation of adverse effects especially of a drug with small therapeutic index, whenever over- medication occurs.

In order to overcome the drawbacks of conventional drug delivery systems, several technical advancements have led to the development of sustained and controlled drug delivery system. Brahmankar et al (2000)

TABLETS

Tablets may be defined as solid pharmaceutical dosage forms containing drug substances with or without suitable diluents and have been traditionally prepared by either compression, or molding methods. The term compressed tablet was used first by John Wyeth and brother of Philadelphia. During the same period, molded tablets were introduced to be used as hypodermic tablets for the extemporaneous preparations of solutions for injections.

COMPRESSED TABLETS

For medicinal substances, with or without diluents, to be made into solid dosage forms with pressure, using available equipment, it is necessary that the material, either in crystalline or powdered form, possesses a number of physical characteristics. These characteristics include the ability to flow freely, cohesiveness and lubrication. The ingredients such as disintegrants design to break the tablet up in GIT fluids and sustained release polymers designed to slow drug release ideally should possess these characteristics or not interfere with the desirable performance traits of the other excipients. Since most materials have none or some of these properties, methods of tablet formulations and preparation have been developed to impart these desirable characteristics to the material that is to be compressed into tablets.

Direct Compression

As the name implies, direct compression consists of compressing tablets directly from powdered material without modifying the physical nature of the material itself. Formerly, direct compression as a method of tablet manufacture was reserved for a small group of crystalline chemicals having all the physical characteristics required for the formation of a good tablet.

Since the pharmaceutical industries constantly is making efforts to increase the efficiency of tableting operations and reduce costs by using the smallest amount of floor space and labor as possible for a given operation, so an increased attention is being given to this method of tablet preparation. Approaches being used to make this method more universally applicable include the introduction of formulation additives capable of imparting the characteristics required for compression and the use of force feeding devices to improve the flow of powder

blends.

Wet Granulation
The most widely used and most general method of tablet preparation is the wet granulation method. Its popularity is due to the greater probability that the granulation will meet all the physical requirements for the compression of good tablets. Its chief disadvantage is the number of separate steps involved, as well as the time and labor necessary to carry out the procedure, especially on the large scale.

Hot Melt Granulation
Melt granulation is one of the most widely applied processing techniques in the array of pharmaceutical manufacturing operations. Melt granulation process is currently applied in the pharmaceuticals for the manufacture of variety of dosage forms and formulation such as immediate release and sustained release pellets, granules and tablets.

SUSTAINED RELEASE Jain Kewal, (2008)
Sustained-release (SR) preparations are not new,but several new modifications are being introduced. They are also referred to as "long-acting" or "delayed- release" as compared to "rapid" or "conventional" release preparations. The term sometimes overlaps with "controlled release"which implies more sophisticated control of release and not just confined to the time dimension. Controlled release implies consistency, but release in SR preparations may not be consistent.

The rationales of developing SR are:
- To extend the duration of action of the drug
- To reduce the frequency of dosing
- To minimize the fluctuations in plasma level
- To improve drug utilization Limitations of SR products are:
- Increase of drug cost
- Variation in the drug-level profile with food intake and from one subject to another
- The optimal release from is not always defined, and multiplicity of SR form may confuse the physician as well as the patient SR is achieved by either chemical modification of the drug or modifying the deli

METHODS USED TO ACHIEVE SUSTAINED RELEASE
Diffusion Controlled System
1 **Reservoir type**: It consists of a core of drug surrounded by polymer membrane, which controls the release rate.
2 **Matrix type**: Matrix system is characterized by a homogenous dispersion of solid drug in a polymer mixture.

Methods using Ion Exchange
It is based on the drug resin complex formation when an ionic solution is kept in contact with ionic resins. The drug from these complexes gets exchanged in gastrointestinal tract and released with excess of Na+ and Cl- present in gastrointestinal tract.

Methods using Osmotic Pressure
It is characterized by drug surrounded by semi permeable membrane and release governed by osmotic pressure.

pH– Independent Formulations
A buffered controlled release formulation is prepared by mixing a basic or acidic drug with one or more buffering agents, granulating with appropriate pharmaceutical excipients and coating with GI fluid permeable film forming polymer. When GI fluid permeates through the membrane the buffering agent adjusts the fluid inside to suitable constant pH thereby rendering a constant rate of drug release.

Altered density formulations
Several approaches have been developed to enhance the residence time of drug delivery system in the gastro intestinal tract.

High density approach Low density approach
In sustained-release formulations employing dissolution as the rate- limiting step, drug release is controlled by dissolution of a polymer or by a chemical reaction with a soluble subunit. Individual particles or granules containing a drug can be uniformly dispersed in the matrix or coated with varying thicknesses of coating material resulting in dissolution and release of the drug over extended periods of time. If the dissolution process is assumed to be diffusion-layer controlled, in which the rate of diffusion from the solid surface to the bulk solution is rate- limiting, the flux is the product of the diffusion coefficient and the concentration gradient from the solid surface to the bulk solution side. Flux can also be defined as the flow rate of material through a unit area. Ranade et al (2011)

With encapsulated dissolution control, the drug may be coated with slowly dissolving polymeric materials. Once the polymeric membrane has dissolved, the entire drug inside the membrane is immediately available for dissolution and absorption. Thus, drug release can be controlled by adjusting the thickness and the dissolution rate of the polymeric membrane. Ranade et al (2011)

MATRIX SYSTEM
A matrix system consists of active and inactive ingredients that are homogeneously mixed in the dosage form. It is by far the most commonly used oral controlled release technology, and the popularity of matrix systems can be attributed to several factors.
- First, unlike reservoir and osmotic systems, products based on matrix design can be manufactured using conventional processing and equipment.
- Second, development time and cost associated with a matrix system generally are viewed as favorable, and no additional capital investment is required.

Lastly, a matrix system is capable of accommodating both low and high drug load and active ingredients with a wide range of physical and chemical properties. Xiaoling et al (2006)

Hydrophillic polymers
Hydroxy (HPMC), propyl Hydroxy methyl propyl cellulose (HPC), ethyl cellulose (EC), methylcellulose (MC), carboxy methylcellulose (CMC), polyvinyl pyrrolidone (PVP) and polyethylene glycol (PEG).

Hydrophobic polymers
These ingredients include waxes, glycerides, fatty acids, and polymeric materials such as ethylcellulose and methacrylate copolymers Waxes and lipids such as carnauba wax, glycerol derivatives as glyceryl mono stearate, glyceryl behenate, glyceryl mono oleate, etc. Quadir et al (2003) The physical characteristics of these waxes and lipids depends upon their structure (length of chain, no. of double bonds) changing their fusion point or their capability to be digested. Ozyazici et al (2006)

MECHANISM OF DRUG RELEASE FROM MATRIX
TABLETS Patel Harnish et al (2011), Costa et al (2001)
Drug in the outside layer exposed to the bathing solution is dissolved first and then diffuses out of the matrix. This process continues with the interface between the bathing solution and the solid drug moving toward the interior. It follows that for this system to be diffusion controlled, the rate of dissolution of drug particles within the matrix must be much faster than the diffusion rate of dissolved drug leaving the matrix.

Derivation of the mathematical model to describe this system involves the following assumptions:

a) A pseudo-steady state is maintained during drug release,
b) The diameter of the drug particles is less than the average distance of drug diffusion through the matrix,
c) The bathing solution provides sink conditions at all times.

The release behavior for the system can be mathematically described by the following equation:
$dM/dh = C_O . dh - C_S/2$

Eqn. (1.3)
When the amount of drug is in excess of the saturation concentration then,
$M = [2C_S.D_M.C_O.t]^{½}$

Where,
dM = Change in the amount of drug released per unit area
dh = Change in the thickness of the zone of matrix that has been depleted of drug
C_O = Total amount of drug in a unit volume of matrix
C_S = Saturated concentration of the drug within the matrix.
Additionally, according to diffusion theory:
$dM = (D_M.C_S /h) dt$
Eqn. (1.4)

Where,
D_m = Diffusion coefficient in the matrix
h = Thickness of the drug-depleted matrix
dt = Change in time
By combining both equations and integrating,
$M = [C_S. D_m (2C_O - C_S) t]^{½}$
Eqn. (1.5)
Eqn. (1.6)

Equations 1.5 & 1.6 relate the amount of drug release to the square-root of time.

Therefore, if a system is predominantly diffusion controlled, then it is expected that a plot of the drug release vs. square root of time will result in a straight line. Drug release from a porous monolithic matrix involves the simultaneous penetration of surrounding liquid, dissolution of drug and leaching out of the drug through tortuous interstitial channels and pores.

The volume and length of the openings must be accounted for in the drug release from a porous or granular matrix:
$M = [D_S. C_a. p/T. (2C_O - p.C_a) t]^{½}$
Eqn. (1.7)

Where,
p = Porosity of the matrix t = Tortuosity
C_a = solubility of the drug in the release medium
D_S = Diffusion coefficient in the release medium
T = Diffusional path length

For pseudo steady state, the equation can be written as-
$M = [2D.C_a .C_O (p/T) t]^{½}$
Eqn. (1.8)

The total porosity of the matrix can be calculated with the following equation-
$p = p_a + C_a/ \rho + C_{ex} / \rho_{ex}$
Eqn. (1.9)

Where,
p = Porosity
ρ = Drug density
p_a = Porosity due to air pockets in the matrix
ρ_{ex} = Density of the water soluble excipients
C_{ex} = Concentration of water soluble excipients

For the purpose of data treatment, equation 1.9 can be reduced to-
$M = k. t^{½}$
Eqn. (1.10)

Where,
k is a constant, so that the amount of drug released versus the square root of time will be linear, if the release of drug from matrix is diffusion-controlled. If this is the case, the release of drug from a homogeneous matrix system can be controlled by varying the following parameters-

- Initial concentration of drug in the matrix
- Porosity
- Tortuosity
- Polymer system forming the matrix
- Solubility of the drug.

EFFECT OF RELEASE LIMITING FACTOR ON DRUG RELEASE Patel Harnish et al (2011)

- **Polymer Hydration:** It is important to study polymer hydration/swelling process for the maximum number of polymers and polymeric combinations. The more important step in polymer dissolution include absorption/adsorption of water in more accessible places, rupture of polymer-polymer linking with the simultaneous forming of water-polymer linking, separation of polymeric chains, swelling and finally dispersion of polymeric chain in dissolution medium.
- **Drug solubility:** Molecular size and water solubility of drug are important determinants in the release of drug from swelling and erosion controlled polymeric matrices. For drugs with reasonable aqueous solubility, release occurs by dissolution in infiltrating medium and for drugs with poor solubility release occurs by both dissolution of drug and diffusion of drug particles through erosion of the matrix.
- **Solution solubility:** All the in vitro drug release studies should also be conducted under perfect sink condition. In this way a better simulation and correlation of in vitro drug release profile with in vivo drug administration can be achieved. It is necessary to maintain a sink condition so that the release of drug gets sustained solely by the delivery system and is not affected or complicated by solubility factor.
- **Polymer diffusivity:** The diffusion of small molecules in polymer structure is energy activated process in which the diffusant molecules moves to a successive series of equilibrium position when a sufficient amount of energy of activation for diffusion has been acquired by the diffusant and is dependent on length of polymer chain segment, cross linking and crystallinity of polymer.

BIOLOGICAL FACTORS INFLUENCING RELEASE FROM MATRIX TABLET Patel Harnish et al (2011)

- **Biological half-life:** The usual goal of an oral sustained release product is to maintain therapeutic blood levels over an extended period of time. To achieve this, drug must enter the circulation at approximately the same rate at which it is eliminated. The elimination rate is quantitatively described by the half-life ($t^{1/2}$). Therapeutic compounds with short half-life are generally excellent candidate for Sustained release formulation, as this can reduce dosing frequency.
- **Absorption:** Since the purpose of forming a SR product is to place control on the delivery system, it is necessary that the rate of release is much slower than the rate of absorption. If we assume that the transit time of most drugs in the absorptive areas of the GI tract is about 8-12 hours, the maximum half-life for absorption should be approximately 3-4 hours; otherwise, the device will pass out of the potential absorptive regions before drug release is complete.
- **Metabolism:** Drugs those are significantly metabolized before absorption, either in the lumen or the tissue of the intestine, can show decreased bioavailability from slower-releasing dosage form. Hence criteria for the drug to be used for formulating Sustained- Release dosage form is, Drug should have low half-life (<5 hrs.) Drug should be freely soluble in water Drug should have larger therapeutic window Drug should be absorbed throughout the GIT Even a drug that is poorly water soluble can be formulated in Sustained release dosage form. For the same, the solubility of the drug should be increased by the suitable system.
- **Distribution:** Drugs with high apparent volume of distribution, which influence the rate of elimination of the drug, are poor candidate for oral Sustained release drug delivery system e.g. Chloroquine.
- **Protein Binding:** The Pharmacological response of drug depends on unbound drug concentration drug rather than total concentration. Proteins binding of drug play a significant role in its therapeutic effect regardless the type of dosage form as extensive binding to plasma increase biological half-life.
- **Margin of safety:** As we know larger the value of therapeutic index safer is the drug. Drugs with less therapeutic index are usually poor candidate for formulation of oral sustained release drug delivery system due to technological limitation of control over release rates.

PHYSICOCHEMICAL FACTORS INFLUENCING RELEASE FROM MATRIX TABLET Patel Harnish et al (2011)

- **Dose size:** For orally administered systems, there is an upper limit to the bulk size of the dose to be administered. In general, a single dose of 0.5-1.0g is considered maximal for a conventional and sustained release dosage form. Compounds that require large dosing size can sometimes be given in multiple amounts or formulated into liquid systems.
- **Ionization, pKa and Aqueous Solubility:** Most drugs are weak acids or bases. Since the unchanged form of a drug preferentially permeates across lipid membranes, it is important to note the relationship

between the pka of the compound and the absorptive environment. Delivery systems that are dependent on diffusion or dissolution will likewise be dependent on the solubility of the drug in aqueous media.

- **Partition Coefficient:** When a drug is administered to the GI tract, it must cross a variety of biological membranes to produce a therapeutic effect in another area of the body. It is common to consider that these membranes are lipidic, therefore the partition coefficient of oil-soluble drugs becomes important in determining the effectiveness of membrane barrier penetration.

MATRIXFORMING HYDROPHOBIC POLYMER

Matrix delivery systems utilizing waxy materials usually employ a core of drug embedded in the wax or a compressed physical blend of drug and matrix- forming agent. As the system passes through the gastrointestinal tract (GIT), the active ingredient is slowly released and absorbed. Since they are water- insoluble and non-swellable, waxy materials have been introduced to eliminate the effects of food present in the GIT on the matrix tablets. Obaidat Aiman et al (2001)

When lipophilic matrix tablets are placed in dissolution media, several cracks, channels, and pores are reportedly formed on their surface. These channels are formed due to a rapid dissolution of the drug particles present on the surface of the matrix. The dissolution medium enters the channels, allowing more dissolution of the drug present at deeper sites of the matrix and leaching the dissolved drug through these channels. Abd El Halim et al (2010)

EXCIPIENT PROFILE Rowe
Raymond et al (2006)

GLYCERYL BEHENATE

- **Synonyms**

Compritol 888 ATO, 2,3- dihydroxypropyl docosanoate, docosanoic acid, 2,3-dihydroxypropyl ester, glycerol behenate, glyceryl monobehenate. Tribehenin is used as a synonym for glyceryl tribehenate.

- **Chemical Name**

Docosanoic acid, monoester with glycerin (glyceryl behenate)
Docosanoic acid, diester with glycerin (glyceryl dibehenate)
Docosanoic acid, triester with glycerin (glyceryl tribehenate)

- **Empirical Formula and Molecular Weight**

The PhEur 2005 describes glyceryl dibehenate as a mixture of diacylglycerols, mainly dibehenoylglycerol, together with variable quantities of mono- and triacylglycerols.

The USPNF 23 describes glyceryl behenate as a mixture of glycerides of fatty acids, mainly behenic acid. It specifies that the content of 1- monoglycerides should be 12.0–18.0%.

- **Functional Category**

Coating agent; tablet binder; tablet and capsule lubricant.

- **Uses**

Table 1.1: Uses of Glyceryl Behenate.

USES	CONCENTRATION (%)
Lipophilic matrix or coating for sustained- released tablets and capsules	>10.0
Tablet and capsule lubricant	1.0–3.0
Viscosity- increasing agent in silicon gels (cosmetics)	1.0–15.0
Viscosity- increasing agent in w/o or o/w emulsions (cosmetics)	1.0–5.0

- **Pharmaceutical Applications**

Glyceryl behenate is used in cosmetics, foods, and oral pharmaceutical formulations. In cosmetics, it is mainly used as a viscosity-increasing agent in emulsions. In pharmaceutical formulations, glyceryl behenate is mainly used as a tablet and capsule lubricant and as a lipidic coating excipient. It has been investigated for the encapsulation of various drugs such as retinoids. It has also been investigated for use in the preparation of sustained release tablets as a matrix-forming agent for the controlled release of water- soluble drugs and as a lubricant in oral solid dosage formulations and it can also be used as a hot-melt coating agent sprayed onto a powder.

- **Description**

Glyceryl behenate occurs as a fine white powder or hard waxy mass with a faint odor.

- **Properties**

Melting point: 65–77°C
Solubility: Soluble, when heated, in chloroform and dichloromethane, practically insoluble in ethanol (95%), hexane, mineral oil, and water.

➢ **Stability and Storage Conditions**
Glyceryl behenate should be stored in a tight container, at a temperature less than 35℃.

➢ **Safety**
Glyceryl behenate is used in cosmetics, foods and oral pharmaceutical formulations and is generally regarded as a relatively nonirritant and nontoxic material.

➢ **Handling Precautions**
Observe normal precautions appropriate to the circumstances and quantities of material handled. Glyceryl behenate emits acrid smoke and irritating fumes when heated to decomposition.

- GRAS listed.

LACTOSE

➢ **Chemical Name**
O-β-D-Galactopyranosyl-(1-4)-α-D- glucopyranose monohydrate.

➢ **Empirical Formula and Molecular Weight**
$C_{12}H_{22}O_{11}.H_2O$ 360.31.

➢ **Functional Category**
Binding agent, diluent for dry-powder inhalers, tablet binder, tablet and capsule diluent.

➢ **Pharmaceutical Applications**
Lactose is widely used as a filler or diluent in tablets and capsules, and to a more limited extent in lyophilized products and infant formulas. Lactose is also used as a diluent in dry-powder inhalation. Various lactose grades are commercially available that have different physical properties such as particle size distribution and flow characteristics. Fine grades of lactose are used in the preparation of tablets by the wet-granulation method or when milling during processing is carried out, since the fine size permits better mixing with other formulation ingredients and utilizes the binder more efficiently. Other applications of lactose include use in lyophilized products, where lactose is added to freeze-dried solutions to increase plug size and aid cohesion. Lactose is also used in combination with sucrose (approximately 1: 3) to prepare sugar-coating solutions.

Direct-compression grades of lactose monohydrate are available as granulated/agglomerated α-lactose monohydrate, containing small amounts of anhydrous lactose.

Direct-compression grades are often used to carry lower quantities of drug and this permits tablets to be made without granulation.

➢ **Description**
In the solid state, lactose appears as various isomeric forms, depending on the crystallization and drying conditions, i.e. α-lactose monohydrate, β-lactose anhydrous, and α-lactose anhydrous. The stable crystalline forms of lactose are α-lactose monohydrate, β-lactose anhydrous and stable α-lactose anhydrous.

Lactose occurs as white to off-white crystalline particles or powder. Lactose is odorless and slightly sweet-tasting; α- lactose is approximately 20% as sweet as sucrose, while β-lactose is 40% as sweet.

➢ **Properties**
Melting point: 201–202℃ (for dehydrated α-lactose monohydrate)

➢ **Stability and Storage Conditions**
Mold growth may occur under humid conditions (80% relative humidity and above). Lactose may develop a brown coloration on storage, the reaction being accelerated by warm, damp conditions.

The purities of different lactose can vary and color evaluation may be important, particularly if white tablets are being formulated. Solutions show mutarotation.

It should be stored in a well-closed container in a cool, dry place.

➢ **Incompatibilities**
A Maillard-type condensation reaction is likely to occur between lactose and compounds with a primary amine group to form brown, or yellow-brown-colored products. Lactose is also incompatible with amino acids, aminophylline, amfetamines, and lisinopril.

- GRAS listed

MICROCRYSTALLINE CELLULOSE

➢ **Synonyms**
Avicel, Celex, cellulose gel, Celphere, Ceolus KG, crystalline cellulose, Emcocel, Ethispheres, Fibrocel, Pharmacel, Tabulose, Vivapur.

➢ **Empirical Formula and Molecular Weight**
$(C_6H_{10}O_5)_n$ = 36,000
where n = 220.

➢ **Functional Category**
Adsorbent, suspending agent, tablet and capsule diluents, tablet disintegrant.

➢ **Uses**

Table 1.2: Uses of Microcrystalline Cellulose.

USES	CONCENTRATION (%)
Adsorbent	20–90
Antiadherent	5–20
Capsule binder/diluents	20–90
Tablet disintegrant	5–15
Tablet binder/diluents	20–90

➢ **Pharmaceutical Applications**

Microcrystalline cellulose is widely used in pharmaceuticals, primarily as a binder/diluent in oral tablet and capsule formulations where it is used in both wet-granulation and direct-compression processes. In addition to its use as a binder/diluent, microcrystalline cellulose also has some lubricant and disintegrant properties that make it useful in tableting.

➢ **Description**

Microcrystalline cellulose is purified, partially depolymerized cellulose that occurs as a white, odorless, tasteless, crystalline powder composed of porous particles. It is commercially available in different particle sizes and moisture grades that have different properties and applications.

➢ **Properties**

Melting point: Chars at 260–270℃.

➢ **Stability and Storage Conditions**

Microcrystalline cellulose is stable though hygroscopic material. The bulk material should be stored in a well-closed container in a cool, dry place.

➢ **Incompatibilities**

Microcrystalline cellulose is incompatible with strong oxidizing agents.

- GRAS listed

POVIDONE K-30

➢ **Synonyms**

Kollidon, Plasdone, poly[1-(2-oxo-1-pyrrolidinyl)ethylene], polyvinylpyrrolidone, PVP, 1-inyl-2 pyrrolidinone polymer.

➢ **Chemical Name**

1- Ethenyl-2-pyrrolidinone homopolymer.

➢ **Empirical Formula and Molecular Weight**

$(C_6H_9NO)_n$

2500–3,000,000

For K value = 30, approximate molecular weight = 50,000

➢ **Functional Category**

Disintegrant, dissolution aid, suspending agent, tablet binder.

➢ **Uses**

Table 1.3: Uses of Povidone.

USES	CONCENTRATION (%)
Carrier for drugs	10–25
Dispersing agent	Up to 5
Eye drops	2–10
Suspending agent	Up to 5
Tablet binder, tablet diluent, or coating agent	0.5-5

➢ **Pharmaceutical Applications**

Although povidone is used in a variety of pharmaceutical formulations, it is primarily used in solid-dosage forms. In tableting, povidone solutions are used as binders in wet granulation processes. Povidone is also added to powder blends in the dry form and granulated in situ by the addition of water, alcohol, or hydroalcoholic solutions. Povidone is used as a solubilizer in oral and parenteral formulations and has been shown to enhance dissolution of poorly soluble drugs from solid-dosage forms. Povidone solutions may also be used as coating agents.

Povidone is additionally used as a suspending, stabilizing, or viscosity- increasing agent in a number of topical and oral suspensions and solutions. The solubility of a number of poorly soluble active drugs may be increased by mixing with povidone. Special grades of pyrogen-free povidone are available and have been used in parenteral formulations.

➢ **Description**

Povidone occurs as a fine, white to creamy-white colored, odorless or almost odorless, hygroscopic powder. Povidone with K-values equal to or lower than 30 are manufactured by spray-drying and occurs as spheres.

➢ **Properties**

Melting point: Softens at 150℃.

➢ **Stability and Storage Conditions**

Povidone darkens to some extent on heating at 150℃, with a reduction in aqueous solubility. It is stable to a short cycle of heat exposure around 110– 130℃, steam sterilization of an aqueous solution does not alter its properties. Aqueous solutions are susceptible to mold growth and consequently require the addition of suitable preservatives.

Povidone may be stored under ordinary conditions without undergoing decomposition or degradation. However, since the powder is hygroscopic, it should be stored in an airtight container in a cool, dry place.

➢ **Incompatibilities**

Povidone is compatible in solution with a wide range of inorganic salts, natural and synthetic resins, and other chemicals. It forms molecular adducts in solution with sulfathiazole, sodium salicylate, salicylic acid, phenobarbital, tannin, and other compounds.

TALC

➢ **Synonyms**

Altalc, hydrous magnesium calcium silicate, hydrous magnesium silicate, magnesium hydrogen Metasilicate, Magsil Osmanthus, Magsil Star, powdered talc, purified French chalk, Purtalc, soapstone.

➢ **Empirical Formula and Molecular Weight**

Talc is a purified, hydrated, magnesium silicate, approximating to the formula $Mg_6(Si_2O_5)_4(OH)_4$. It may contain small, variable amounts of aluminum silicate and iron.

➢ **Functional Category**

Anticaking agent, glidant, tablet and capsule diluents, tablet and capsule lubricant.

➢ **Uses**

Table 1.4: Uses of Talc.

USES	CONCENTRATION (%)
Dusting powder	90.0–99.0
Glidant and tablet	1.0–10.0
lubricant	
Tablet and capsule diluents	5.0–30.0

➢ **Pharmaceutical Applications**

Talc was once widely used in oral solid dosage formulations as a lubricant and diluents. Although today it is less commonly used. However, it is widely used as a dissolution retardant in the development of controlled-release products. Talc is also used as a lubricant in tablet formulations, in a novel powder coating for extended-release pellet and as an adsorbent.

In topical preparations, talc is used as a dusting powder, although it should not be used to dust surgical gloves. Talc is a natural material, it may therefore frequently contain microorganisms and should be sterilized when used as a dusting powder, and Talc is additionally used to clarify liquids and is also used in cosmetics and food products, mainly for its lubricant properties.

➢ **Description**

Talc is a very fine, white to grayish- white, odorless, impalpable, unctuous, crystalline powder. It adheres readily to the skin and is soft to the touch and free from grittiness.

➢ **Properties**

Solubility: Practically insoluble in dilute acids and alkalis, organic solvents, and water.

➢ **Stability and Storage Conditions**

Talc is a stable material and may be sterilized by heating at 160℃ for not less than 1 hour. It may also be sterilized by exposure to ethylene oxide or gamma irradiation.

Talc should be stored in a well-closed container in a cool, dry place.

➢ **Incompatibilities**

Incompatible with quaternary ammonium compounds.

CONCLUSION

In the present investigation an attempt has been made to design and develop Captopril sustained release matrix tablets by three different techniques namely direct compression, wet granulation and hot melt granulation. Captopril is an antihypertensive drug which lowers the blood pressure level in the body. Compritol (glyceryl behenate) was selected to control the release rate of drug from the matrix. It can be easily that sustained-release formulation are helpful in increasing the efficiency of the dose as well as they are also improved the patients co.

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