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A Review: Extended Release Tablet

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Abstract:

The extended release Tablet became a very useful tool in medical practice, it gives lot of advantages to the patients. Oral extended release tablet release the drug at predetermined rate over a long period of time so the it reduces the frequency of dose administration and increase the patient compliance. Extended release is reduce the side effect or adverse effect of the drug by reducing or preventing the fluctuation of the plasma drug concentration or therapeutic concentration of the drug in the body. This review focus on the types of ER tablets, Method of preparation of tablets, defects in tablets, mechanisms involved for release of drug in extended release tablets and advantages of ER tablets over conventional tablet.

Key word: Extended release, Tablet, Concentration, Defects, Granules, Coating etc.,

1. INTRODUCTION

1.1. Tablet [1]:

A tablet is a pharmaceutical dosage form. Tablets could also be defined because the solid unit dosage sort of medicament or medicaments with or without suitable excipients and ready either by molding or by compression. It comprises a mix of active substances and excipients, usually in powder form, pressed or compacted from a powder into a solid dose. The excipients can include diluents, binders or granulating agents, glidants (flow aids) and lubricants to make sure efficient tableting; disintegrants to market tablet break-up within the digestive tract; sweeteners or flavors to enhance taste; and pigments to make the tablets visually attractive or aid in visual identification of an unknown table Oral solid dosage forms (tablets) are having better advantages compared with other dosage forms in both handling and administration. These are having certain properties which include the dose and weight uniformity, the strength (i.e., the tensile strength and friability-especially in tablet and pellets), disintegration and drug release. Tablets are often made in virtually any shape, although requirements of patients and tableting machines mean that the majority are round, oval or capsule shaped. Tablets got to be strong enough to resist the stresses of packaging, shipping and handling by the pharmacist and patient. Tablets are solid dosage form manufactured either by dry granulation, wet granulation or direct compression containing medicaments with or without excipients, intended to supply desired pharmacological response. Various types of tablets are being manufactured according the route of administration and type of dosage form.

1.1.1. Commonly used excipients in tablet preparation

1. **Diluents:** Diluents are normally used as a fillers, in order to increase the bulk of the tablet. Example for diluents includes lactose, starch, mannitol etc.

2. **Binders and adhesives:** Binders are either added in wet form or dry form, which serves as a binding agent in the formulation. Commonly used binders include starch, carboxy methyl cellulose. The type of the binder added vary with the formulation. The amount of binder added and type of binder influences the tablet properties.

3. **Disintegrants:** These are added, in order to aid in disintegration or breaking of tablet in GIT. Disintegrants like starch, clays, cellulose are used.

4. **Lubricants:** Lubricants prevents sticking of tablets to dies and punches. : Talc, stearic acid, magnesium stearate.

5. **Glidants:** They reduce the friction, thus aid in free flow of granules or powder. Commonly used glidants includes starch and talc.

6. **Colouring agents:** Helps in elegant appearance of the product. Examples of colouring agents like brilliant blue.

7. **Sweeting agent:** Sweeting agent are added in order to mask the bitter taste of the drug. Ex: aspartame, mannitol, lactose

8. **Flavouring agent:** Added in order to impart flavour or odour to the table formulation. Ex: Menthol, clove oil, vanilla.

1.1.2. Types of tablets [1]

- Film coated tablet.
- Sugar coated tablet
- Chewable tablet
- Compressed tablet
- Multiple compressed tablet
- Enteric coated tablet
- Immediate release tablet
- Extended release tablet
- Bilayer tablet

1.1.2.1. Film-coated tablets (FCT): These are compressed tablets covered with a skinny layer or film of a water soluble material. variety of polymeric substances could also be used for film coating. Film coating imparts the identical general characteristics as sugar coating, additionally it offers reduced period required for the coating operation.

1.1.2.2. Sugar coated tablets: These are compressed tablets which are coated with sugar, so as to mask the bitter taste or odor of the drug.

1.1.2.3. Chewable tablet: These tablets are placed to mouth which are chewed and swallowed. Chewable tablets are a convenient alternative to standard tablets. they need the good advantage of not requiring water, which suggests that they will be taken at any time and in anyplace. When employed in combination with other dosage forms, like effervescent tablets, chewable tablets offer additional variety for patients, improving the experience and ensuring better compliance.

1.1.2.4. Compressed Tablets (CT): These tablets are prepared by compression technique during which tablets aren't coated with any material.

1.1.2.5. Multiple Compressed Tablets (MCT): These tablets are subjected to over one compression cycle.

1.1.2.6. Enteric-Coated Tablets (ECT): An enteric coating may be a polymer barrier applied on oral medication that stops its dissolution or disintegration within the gastric environment. This helps by either protecting drugs from the acidity of the stomach, the stomach from the detrimental effects of the drug, or to release the drug after the stomach (usually within the upper tract of the intestine). Some drugs are unstable at the acid gastric pHand have to be shielded from degradation. Enteric coating is additionally a good method to get drug targeting (such as gastro-resistant drugs). Other drugs like some anthelmintic may have to succeed in a high concentration during a specific a part of the intestine.

1.1.2.7. Oral Immediate Release Tablet [2]: The term "immediate release" pharmaceutical formulation includes any formulation during which the speed of release of drug from the formulation and/or the absorption of drug, is neither appreciably, nor intentionally, retarded by galenic manipulations.

1.1.2.7.1. An on the spot release pharmaceutical preparation offers:

- Improved compliance/added convenience
- Improved stability.
- Suitable for controlled/sustained release actives
- Ability to produce advantages of liquid medication within the variety of solid preparation.
- Adaptable and amenable to existing processing and packaging machinery
- Cost- effective.

1.1.2.7.2. Desired criteria for immediate release drug delivery system

Immediate release dosage form should- within the case of solid dosage it should dissolve or disintegrate within the stomach within a brief period. within the case of liquid dosage form it should be compatible with taste masking.

- Portable without fragility concern.
- Have a satisfying mouth feel.
- It shouldn't leave minimal or no residue within the mouth after oral administration.
- Exhibit low sensitivity to condition as humidity and temperature.
- Be manufactured using conventional processing and packaging equipment at low cost.
- Rapid dissolution and absorption of drug, which can produce rapid onset of action.

1.1.2.8. Oral Extended Release Tablet [3,4]: The oral controlled release dosage forms are designed to realize a chronic therapeutic effect by continuously releasing medication over an extended period of your time after administration of one dose that may provide reproducible and effective plasma concentrations in vivo. Modified-release formulation technologies offer a good means to optimize the bioavailability and resulting blood concentration-time profiles of the drugs. Modified release will be categorized into delayed release and extended or prolonged release. Sustained release products aim is releasing the drug continuously at a predetermined rate and time so as to extend the patient compliance. This can be expected since the frequency of administration is reduced and peaks are move prevent high concentrations, locally or systemically, which may cause undesirable side effects. Thus, the tissue concentrations are kept at a coffee but effective level over an extended period of your time.

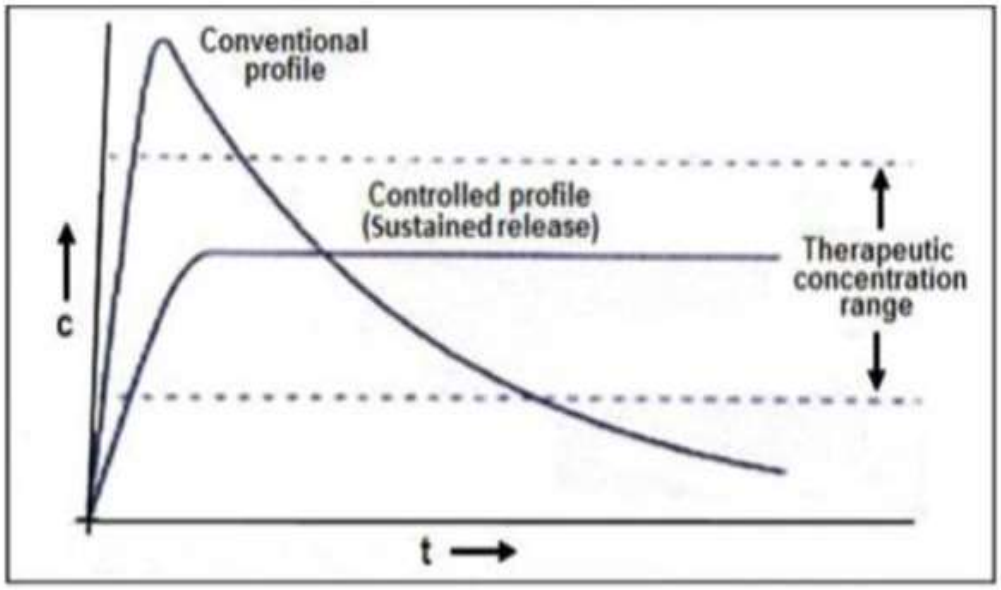

Figure No 1: Comparative release pattern of conventional and modified release dosage forms.

Showing maximum safe concentration (MSC) and minimum effective concentration (MEC) These are the kind of extended drug delivery systems, which release the drug in continuous manner by both dissolution controlled further as diffusion controlled mechanisms. to manage the discharge of the drugs, which are having different solubility properties, the drug is dispersed in swellable hydrophilic substances, an insoluble matrix of rigid non swellable hydrophobic materials or plastic materials. Chronic pain remains a significant societal burden that's related to a decline of normal daily functioning and quality of life. it's defined as pain that lasts longer than three months and which isn't in relation with any somatic damage.

1.1.2.8.1. Advantages of extended release matrix tablet [5]:

• Easy to manufacture

• Versatile, effective and low cost

• is made to release high mass compounds

• The sustained release formulations may maintain therapeutic concentrations over prolonged periods.

• The employment of sustain release formulations avoids the high blood concentration of drug.

• Sustain release formulations have the potential to boost the patient compliance.

• Reduce the toxicity by slowing drug absorption.

• Increase the steadiness by protecting the drug from hydrolysis or other derivative changes in digestive tube.

• Minimize the local and systemic side effects.

• Improvement in treatment efficacy.

• Minimize drug accumulation with chronic dosing.

• Usage of less total drug.

• Improvement the bioavailability of some drugs.

• Improvement of the flexibility to supply camera work. Ex: Morning relief of arthritis through bed time dosing.

1.1.2.8.2. Disadvantages of extended release matrix tablet [5]:

Disadvantages of extended release matrix tablet are as follow,

• The remaining matrix must be removed after the drug has been released.

• High cost of preparation.

• The discharge rates are stricken by various factors like, food and therefore the rate transit through the gut.

• The drug release rates vary with the root of your time.

Release rate continuously diminishes because of a rise in diffusional resistance and/or a decrease in effective area at the diffusion front. However, a considerable sustained effect is produced through the employment of very slow release rates, which in many applications are indistinguishable from zero-order.

1.1.2.8.3. Classification of extended release matrix tablet [5]: Classification of extended release matrix tablet is as follow, On the idea of retardant material Used, extended release matrix tablets is divided in to 5 types.

a. Hydrophobic matrices (Plastic matrices): The concept of using hydrophobic or inert materials as matrix materials was first introduced in 1959. During this method of obtaining sustained release from an oral dosage form, drug is mixed with an inert or hydrophobic polymer so compressed in to a tablet. Extended release is produced because of the actual fact that the dissolving drug has diffused through a network of channels that exist between compacted polymer particles. samples of materials that are used as inert or hydrophobic matrices include polyethylene, PVC, ethyl cellulose and acrylate polymers and their copolymers. The rate-controlling step in these formulations is liquid penetration into the matrix. The possible mechanism of release of drug in such form of tablets is diffusion. Such forms of matrix tablets become inert within the presence of water and gastrointestinal fluid.

b. Lipid matrices: These matrices prepared by the lipid waxes and related materials. Drug release from such matrices occurs through both pore diffusion and erosion. Release characteristics are therefore more sensitive to digestive juice composition than to totally insoluble polymer matrix. wax together with stearyl alcohol or saturated fatty acid has been utilized for retardant base for several sustained release formulations.

c. Hydrophilic matrices: Hydrophilic polymer matrix systems are widely utilized in oral controlled drug delivery thanks to their flexibility to get a desirable drug release profile, cost effectiveness, and broad regulatory acceptance. The formulation of the drugs in gelatinous capsules or more frequently, in tablets, using hydrophilic polymers with high gelling capacities as base excipients is of particular interest within the field of controlled release. Infact a matrix is defined further mixed composite of 1 or more drugs with a gelling agent (hydrophilic polymer). These systems are called swellable controlled release systems. The polymers utilized in the preparation of hydrophilic matrices are divided in to 3 broad groups,

• Various Cellulose derivatives utilized in extended release matrix tablet are as follow, methylcellulose 400 and 4000cPs, hydroxyethylcellulose; hydroxypropylmethylcellulose (HPMC) 25, 100, 4000 and 15000cPs; and sodium

carboxymethylcellulose etc.

• Non cellulose natural or semi synthetic polymers utilized in extended release matrix tablet are as follow, agar-agar; carob gum; alginates; molasses; polysaccharides of mannose and galactose, chitosan and modified starches

• Polymers of carboxylic acid utilized in extended release matrix tablet are as follow,Carbopol934, the foremost used variety.

d. Biodegradable matrices: These accommodates the polymers which comprised of monomers linked to 1 another through functional groups and have unstable linkage within the backbone. they're biologically degraded or eroded by enzymes generated by surrounding living cells or by non-enzymetic process in to oligomers and monomers which will be metabolized or excreted. Examples are natural polymers like proteins and polysaccharides; modified natural polymers; synthetic polymers like aliphatic poly (esters) and poly anhydrides.

e. Mineral matrices: These accommodates polymers which are obtained from various species of seaweeds. Example is gum which may be a hydrophilic carbohydrate obtained from species of brown seaweeds (Phaephyceae) by the employment of dilute alkali.

1.1.2.8.4. On the premise of porosity of matrix employed in formulation [5]: Matrix system can even be classified in keeping with their porosity and consequently, macro porous; micro porous and non-porous systems are often identified:

a. Macro porous systems are as follow, In such systems the diffusion of drug occurs through pores of matrix, which are of size range 0.1 to 1 μm. This pore size is larger than diffusant molecule size.

b. Micro porous system is as follow, Diffusion during this style of system occurs essentially through pores. For micro porous systems, pore size ranges between 50 – 200 A°, which is slightly larger than diffusant molecules size.

c. Non-porous system are as follow, Non-porous systems haven't any pores and therefore the molecules diffuse through the network meshes. during this case, only the polymeric phase exists and no pore phase is present.

1.1.2.8.5. Polymers employed in matrix tablet [5]:

a. Various hydrogels are employed in extended release matrix tablet are as follow, Polyhydroxyethylemethylacrylate (PHEMA), cross-linked polyvinyl alcohol. (PVA), crosslinked polyvinyl pyrrolidone (PVP), polyethylene oxide (PEO), polyacrylamide etc.

b. Various soluble polymer are employed in extended release matrix tablet are as follow,Polyethyleneglycol(PEG),polyvinylalcohol(PVA),polyvinylpyrrolidone(PVP),hydrox ypropyl methyl cellulose (HPMC) etc.

c. Biodegradable polymers are employed in extended release matrix tablet are as follow,Polylactic acid (PLA), Polyglycolic acid (PGA), Polycaprolactone(PCL),Polyanhydrides, Polyorthoesters etc.

d. Non-biodegradable polymersare employed in extended release matrix tablet are as follow,Polyethylene vinyl acetate (PVA), Polydimethylsiloxane (PDS), Polyether urethane (PEU), vinyl polymer (PVC), cellulose ester (CA), Ethyl cellulose (EC) etc.

e. Mucoadhesive polymers are employed in extended release matrix tablet are as follow,Polycarbophil, Sodium cellulose, Polyacrylic acid, Tragacanth, Methyl cellulose, Pectin etc. f. Natural gums are employed in extended release matrix tablet are as follow,Xanthan gum, Guar gum, Karaya gum, algarroba gum etc.

1.1.2.8.6. Mechanism of drug release from matrix tablet [6]: Drug within the outside layer exposed to the showering solution is dissolved first and so diffuses out of the matrix. This process continues with the interface between the showering solution and therefore the solid drug moving toward the inside. It follows that for this technique to be diffusion controlled, the speed 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 explain this technique involves the subsequent assumptions:

a. A pseudo-steady state is maintained during drug release,

b. The diameter of the drug particles is a smaller amount than the common distance of drug diffusion through the matrix,

c. the showering solution provides sink conditions the least bit times.

The release behavior for the system are often mathematically described by the subsequent equation, in keeping with diffusion theory:

dM/dh = Co. dh - Cs/2

Where,

dM = Change within the amount of drug released per unit area

dh = Change within the thickness of the zone of matrix that has been depleted of drug

Co = Total amount of drug in a very unit volume of matrix

Cs = Saturated concentration of the drug within the matrix

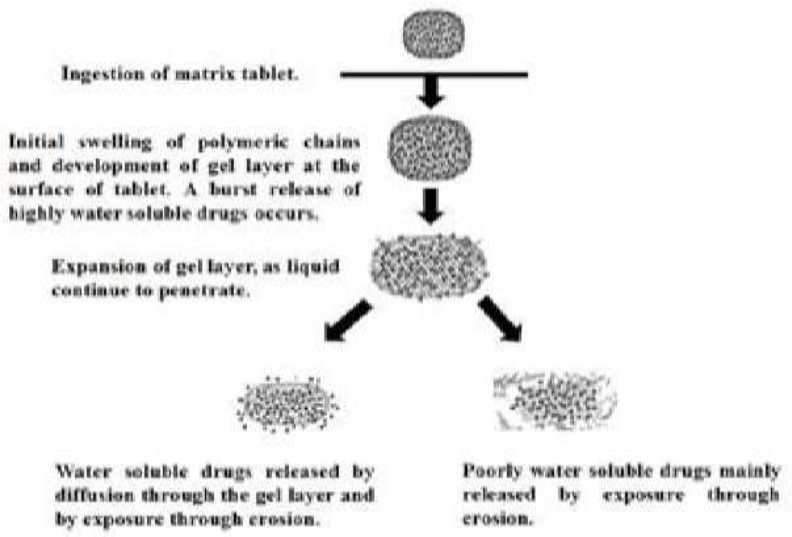

Figure no 2: Mechanism of matrix tablet

1.1.2.8.7. Drug properties relevant to extended release formulations [5]: For designing sustained release delivery systems, variables like the route of drug delivery, the sort of delivery system, the disease to be treated, the length of therapy and also the properties of the drug are to be considered of particular interest to the scientist designing the system are the constraints imposed by the properties of the drug. These properties are classified as:

a. Physicochemical properties

b. Pharmacokinetic properties of drug

These properties have the best effect on the behavior of the drug within the delivery system and within the body. there's no clear-cut distinction between these two categories since the biological properties of a drug are a function of its physicochemical properties. By definition, physicochemical properties are those who are often determined from in vitro experiments. Biological properties are those who result from typical pharmacokinetic studies of the absorption, distribution, metabolism, and excretion (ADME) characteristics of a drug and people resulting from pharmacological studies.

a. Physicochemical properties of the drug for extended release tablet [7]:

Table 1: Physicochemical properties of the drug

Sr. No.	Physicochemical property	Description
1	Dose Size	Less than 0.5 g
2	Solubility criteria	More than 0.1 g/ml. and pH-independent solubility
3	Partition coefficient	Intermediate range of partition coefficient.
4	Drug stability	Should be stable throughout GI tract.
5	Molecular size	Upto 500-700 Daltons.

b. Pharmacokinetic properties of drug [8]: It is a fate of study of drug within the body, right from the time they enter the body until they or their by-product eliminate from the body. Detail knowledge of the ADME characteristics of a drug is important within the design of extended release product. An optimum range of a given pharmacokinetic parameter of a drug is critical, beyond which extended delivery is difficult or impossible.

i. Absorption rate: Drugs that are slowly absorbed or absorbed with a variable absorption rate are poor candidates for an extended release system for oral dosage forms, the lower limit on the absorption rate constant is within the range of 0.25 -1 h (assuming GI transit time of 10-12 h).

ii. Distribution: Drugs with high apparent volumes of distribution, which successively influences the speed of elimination for the drug, are poor candidates.

iii. Rate of metabolism: A drug, which is extensively metabolized, is suitable for controlled release system as long because the rate of metabolism isn't too rapid. The extent of metabolism should be identical and predictable when the drug is run by different routes. A drug capable or inhibiting metabolism may be a poor candidate for such a product since steady blood would be difficult to take care of.

iv. Elimination half-life (t1/2): Smaller the half-life (t½), larger the quantity of drug to be incorporated within the extended release dosage form for drugs with t½ but 2 h, a really large dose is also required to take care of the most release rate. Drugs with half-life within the range of 2-4 h observe candidates for such a system e.g. propranolol, amlodipin and mono-amino oxidase (MAO) inhibitors. In terms of minimum continuance (MRT), drug administered as controlled release dosage form should have MRT significantly longer than conventional dosage forms. v. Margin of safety (Toxicity): it's defined because the ratio of Css maximum to Css minimum. Since the goal of formulation is to enhance therapy by reducing the dosage form index while maintaining the plasma drug levels within the therapeutic window, ideally its value should be as near one as possible. d. Pharmacodynamics properties of the Drug: this is often the experimental study of action of action of drug on the living organism including their mechanism of action.

i. **Therapeutic range:** A drug candidate for extended delivery system should have a therapeutic range wide enough such variations within the release rate don't end in a level beyond this level.
ii. **Therapeutic index (TI):** The discharge rate of a drug should be such the plasma concentration is within the therapeutically safe and effective range. As toxic concentration range is nearer to their therapeutic

range, precise control of release rate of drug with narrow therapeutic index should be administered more frequently than twice on a daily basis. Therapeutic index is given as follows:

T.I. = Lethal dose$_{50}$/ Effective dose$_{50}$

Drugs having broad T.I. value are selected for sustained release formulation.

1.1.2.9. Bilayer tablet [9]: Bi-layer tablets are developed to attain controlled delivery of various drugs with pre-defined release profiles. Bilayer tablet which may provide immediate or sustained release of two drugs or different release rates of the identical drug in one dosage form. The tab letting process can provide an instantaneous release granulate and a modified-release hydrophilic matrix complex as separate layers within the one tablet.

1.2. Introduction to Bilayer Tablet [3,9]: Over the past 30 years because the expense and complications involved in marketing new drug entities have increased, with concomitant recognition of the therapeutic advantages of controlled drug delivery, greater attention has been focused on development of sustained or controlled release drug delivery systems. Bilayer tablet is new era for the successful development of controlled release formulation together with various features to supply some way of successful drug delivery system. Bilayer tablet is best than the traditionally used mouth wash, sprays, and gels. So use of bilayer tablet may be a very different aspect for antiinflammatory and analgesic. Bilayer tablet is improved beneficial technology to beat the short coming of the one layered tablet. There's various application of the bilayer tablet it carries with it monolithic partially coated or multi-layered matrices. In case of bilayer tablets drug release are often rendered almost unidirectional if the drug are often incorporated within the upper non adhesive layer its delivery occurs into the full rime. Usually conventional dosage form produce wide ranging fluctuation in drug concentration within the blood stream and tissues with undesirable toxicity and poor efficiency. This factor like repetitive dosing and unpredictable absorption led to the concept of controlled drug delivery systems. The goal in designing sustained delivery systems is to cut back the frequency of the dosing or to extend effectiveness of the drug by localization at the location of action, reducing the dose required or providing uniform drug delivery. The first objective of sustained release drug delivery is to confirm to boost efficacy of medicine still as patient compliance. Bi-layer tablet is suitable for sequential release of two drugs together, separate two incompatible substances and also for sustained release tablet within which one layer is immediate release as initial dose and second layer is maintenance dose

1.2.1. Advantages of bilayer tablet [3]:

1. Bilayer tablets are often a primary choice to avoid chemical incompatibilities between API by physical separation, and to enable the event of various drug release profiles (immediate release with extended release).

2. Release of both drugs starts immediately; combination of incompatible drugs, Physical/chemical incompatibility are often prevented by physical separation of two drugs. Combination of various release profiles immediate release and sustained release profile are often achieved in single tablet by forming IR layer and ER layer.

3. Reduced Pill Burden by reducing individual dose of two drugs thanks to their additive effect.

4. Bi-layer execution with optional single-layer conversion kit.

5.Greatest chemical and microbial stability over all oral dosage form.

6. just in case of a standard dosage form thanks to fluctuation of the dose interval the plasma drug concentration may differ (under medication or over medication), but during this dosage form the plasma drug concentration is often constant, which ultimately provide a simpler action of the drug.

7. Better control of drug absorption are often attained, since the high blood level peaks which will be observed after administration of a dose of high availability drug are often reduced by formulation in an extended action form. the protection margin of high potency drugs are often increased and therefore the local and systemic adverse effects are often reduced in sensitive patients.

8. Frequency of the dose administration is reduced which ultimately improve the patient compliance.

9. Suitable for giant scale production.

1.2.2. Limitations of bilayer tablet [10]: From the above mentioned advantage of bilayer tablets it's quite clear that in pharmaceutical industry it's an excellent revolution, but there are certain limitations within the formulation and use of bilayer tablets, such as:

1. Drugs with poor wetting, slow dissolution properties, optimum absorption high in GIT could also be difficult to formulate or manufacture as a tablet that may still provide adequate or full drug bioavailability.

2. One amongst the key challenges in bilayer formulation is lack of sufficient bonding and adhesion at the interface between the adjacent compacted layers which is usually the results of an interfacial crack and layer separation.

3. Difficult to swallow just in case of youngsters and unconscious patients.

4. If the compacted layers are too soft or too hard, they'll not bind securely with one another which might result in compromised mechanical integrity and also the separation of the layers.

5. Other challenges during development include establishing the order of layer sequence, layer weight ratio, elastic mismatch of the adjacent layers, first layer tamping force, and cross contamination between layers.

6. The adjacent layers of a bilayer tablet are bonded together by mechanical means, therefore the factors influences the strain state is incredibly important. The mechanical properties of every layer and therefore the tablet, and compression parameters together with specialized techniques and compression condition plays a really important role for the identical.

7. Administration of sustained release bilayer tablet doesn't permit the prompt termination of therapy.

8. Bitter testing drugs, drugs with an objectionable odour or drugs that are sensitive to oxygen may require encapsulation or coating.

9. The physician includes a less flexibility on adjusting the dose regimens.

1.2.3. Types of Bilayer Tablets [11]: The term bilayer tablets containing subunits that will be either the identical (homogeneous) or different (heterogeneous).

1.2.3.1. Homogenous Type: Bilayer tablets are preferred when the discharge profiles of the drugs are different from each other. Bilayer tablets allows for designing and modulating the dissolution and release characteristics. Bilayer tablets are prepared with one layer of drug for immediate release while second layer designed to release drug, later, either as second dose or in an extended release manner.

1.2.3.2. Heterogeneous Type: Bilayer tablet is suitable for sequential release of two drugs together, separate two incompatible substances.

1.2.4. Various techniques for bilayer tablet [11,12]:

1.2.4.1. OROS® push pull technology

This technique encompass mainly two or three layer among which the one or more layer are essential of the drug and other layer are encompass push layer. The drug layer mainly consists of drug together with two or more different agents. So this drug layer comprises of drug which is in poorly soluble form. There's further addition of suspending agent and osmotic agent. A semi-permeable membrane surrounds the tablet core.

1.2.4.2. L-OROS technology

This technique used for the solubility issue. Alza developed the L-OROS system where a lipid soft gel Product containing drug in an exceedingly dissolved state is initially manufactured so coated with a barrier membrane, than osmotic push layer so a semi permeable membrane, drilled with an exit orifice.

1.2.4. ENSOTROL technology

Solubility enhancement of an order of magnitude or to form optimized dosage form Shire laboratory use an integrated approach to drug delivery specializing in identification and incorporation of the identified enhancer into controlled release technologies.

1.2.5. DUROS technology

The system consists from an outer cylindrical titanium alloy reservoir. This reservoir has high impact strength and protects the drug molecules from enzymes. The DUROS technology is that the miniature drug dispensing system that opposes like syringe and regions minute quantity of concentrated forming continues and consistent from over months or year.

1.3. Techniques for Tablet Preparation [13]:

A. Wet granulation method

B. Dry granulation method

C. Direct compression

a. Wet granulation method: It's the foremost common and widely used method. This method involves various steps like weighing of ingredients, mixing, granulation, and screening of damp pass, drying, lubrication and compression of tablets. The most active ingredient, diluent, disintegrants are blended together, then it's allowed to go through the sieve (sifting). Solutions of the binding agent are added to the initial mixture with stirring. The number of binding agent added should be sufficient, so as to avoid over wetting of the tablet. If the powder isn't wetted properly, the granules are going to be too soft and may be softened during lubrication, which is difficult during compression of tablet. Tray drying is most typical method of drying the tablet granules, Tray drying was the foremost widely used method of drying tablet granulations within the past, which could get replaced by FBD as a completely unique approach. After drying the granules, they're allowed to go through the screen, usually 60100 mesh nylon cloth is employed. After dry granulation, lubricant is added as fine powder, which is required for correct filling of the die cavity.

• Important steps involved in wet granulation:

- Mixing of drug(s) and excipients.
- Preparation of binder solution.
- Mixing of binder solution with powder mixture to create wet mass.
- Course screening of wet mass employing a suitable sieve (6-12 screens).
- Drying of moist granules.
- Screening of dry granules through an appropriate sieve (14-20 screen).
- Mixing of screened granules with disintegrants, glidants, and lubricant.

• Special wet granulation techniques

- High shear mixture granulation
- Fluid bed granulation
- Extrusion-spheronization

- Spray drying

b. Dry granulation method: This method is employed for tablet preparation, just in case tablet ingredients are sensitive to moisture, or unable to with stand elevated temperatures during drying, slugging is also wont to form the granules. Dry granulation or double compression, usually eliminates various steps, which involves slugging of the powder mass. The active ingredient, diluent and lubricant are blended together, to create the slug. Thus, the compressed slug is skilled the mesh or through the mill, and also the remaining lubricant is added to the granulation, blended properly and compressed to create the tablets.

c. Direct compression: Direct compression involves direct compressing the powdered material into tablets. Direct compression is adopted, if drug constitutes major portion of tablet total weight. Tablets containing 25% or less of drug substances are often formulated, with an appropriate diluent which acts as a carrier or vehicle for the drug. Tablets prepared by above method are subjected to compression machine which can be single station or multiple station. •

Advantages:

a. Direct compression is more efficient and economical process as compared to other processes, because it involves only dry blending and compaction of API and necessary excipients.

b. the foremost important advantage of direct compression is that it's a cost-effective process. Reduced interval, reduced labour costs, fewer manufacturing steps, and fewer number of equipment's is required, less process validation, reduced consumption of power.

c. Elimination of warmth and moisture, thus increasing not only the soundness but also the Suitability of the method for thermolabile and moisture sensitive API.

1.4. Ideal characteristics of tablets [1]:

A. Should be free from defects like cracks, discoloration, chips etc.

B. Should ready to withstand mechanical stress

C. Physically and chemically stable.

1.5. Manufacturing defects in tablet compression [1]: During processing of tablets during compression, there several processing problems encountered such as: Picking, sticking, capping, lamination, mottling.

A. Picking: The tablet surface material could also be removed by a punch during compression leads to picking.

B. Sticking: Adhesion of tablet to the die wall, which can occur thanks to excessive moisture within the tablet.

C. Capping: It is partial or complete separation of tablet from the highest or bottom crowns of the tablet from the most body.

D. Lamination: Segregation of a tablet into two or more distinct layers. Capping and lamination may occur thanks to air entrapment during processing.

E. Mottling: Unequal distribution of color on tablet surface leads to mottling.

1.6. Coating [1,14,15]: The tablet coating have number of benefits like masking odor, taste, color of the drug, providing physical and chemical protection to drug, Protecting drug from the gastric environment. Three primary components of tablet coating are tablet properties, coating process and coating composition. Tablets are usually coated in horizontal rotating pan with coating solution is either directly poured or sprayed on to them. The number of coating on the surface of a tablet is critical to the effectiveness of the oral dosage form.

1.6.1. Mechanism of coating: The mechanisms by which films are formed from solutions and water-dispersions are fundamentally different. The formation of coatings from solutions involves conversion of a viscous liquid into a viscoelastic solid, which is accomplished in three steps of solvent removal

A. Evaporation of solvent at the surface of the coating

B. Diffusion of solvent from the wet coating to the surface

C. Slow diffusion of residual solvent within the dried coating

1.6.2. Aqueous Film Coating [15]: Aqueous film coating is applied as a skinny polymeric film to the surface of a tablet. Film coating can protect the tablet from light, temperature and moisture, mask undesirable taste or odour, improves the looks, provide tablet identity, facilitate swallowing control or modified the discharge of drug. Aqueous film of oral dosage forms has rapidly replaced solvent based coating for safety, environmental and economic reasons. Since tablet may contain moisture sensitive drugs or excipients, the employment of water raise concerns about the physical and chemical stability of the coated tablet.

1.6.3. Coating equipment [15]: In present study, R and D coater was used for coating purpose using dispersion and solution layering techniques. The Pharma R and D coater is an integrated and automatic / semiautomatic unit consisting of a chrome steel (304/316) coating pan, a spraying

Figure no 3: Conventional coating equipment

system, a hot air blower, and an system are shown in fig. 3. It uses the rotary momentum of the coating pan to tumble the tablets / granules contained with it. Baffles are provided along the inside walls of the pan to tilt the contents for efficient coating.

Conclusion: ER (extended release) tablets shows the better patient compliance through reduction of frequency of dose administration and also maintain the therapeutic concentration over a long period of time it help to reduce the side effect of the drug and goves better effect. The ER tablet is very helpful to treat the chronic diseases.

REFERENCES:

1. Lachman L., Lieberman H.A., Kainig J.L., 1987. The Theory and Practice of Industrial Pharmacy, Varghese Publishing House, Bombay. Third Edition, 336, 413.

2. Bhandari N., Kumar A., 2014. A Review on Immediate Release Drug Delivery System, International Research Journal of Pharmaceutical and Applied Sciences. (1), 78-87.

3. Bhosale M., Kulkarni K., 2017. Bilayer tablet: A Comprhensive Review, European Journal of Pharmaceutical and Medical Research. (4), 241-251.

4. Patel K., Patel S., An Overview: Extended Release Matrix Technology International Journal of Pharmaceutical and Chemical Sciences. (1), 828-843.

5. Chein Y.W., 2002. Novel drug delivery system, Marcel Dekker Inc. New York., (50), 1- 43.

6. Jain N. K., 2004. Controlled and novel drug delivery system, controlled and novel drug delivery system, C B S Publishers and distributors, New Delhi., 419-435.

7. Banker G., Rhodes C., 2002. Modern pharmaceutics, Marcel Dekker Inc, New York. Fourth edition, (121), 306-308.

8. Bramhankar D.M., Jaiswal S.B., 2008. Biopharmaceutics and pharmacokinetics, Vallabh prakashan, Delhi, India, First edition, 335-371.

9. Anusha J., Karthik M., 2016. A Review on Bilayered Tablets, Research and Reviews: Journal of Pharmacy and Pharmaceutical Sciences, (5), 118-124.

10. Chauhan M., Suthar S., 2012. Bilayer tablet: Immediate Release and Sustain Release: A Review, Research Journal of Pharmacy and Technology, (5), 716-720.

11. RaveendraBabu G., Sambasiva R., 2015. Bilayer Tablets-A Review, International Journal of Pharmaceutical, Chemical and Biological Sciences, (3), 510-516.

12. Pateriya A., Joshi A., 2013. Formulation and Evaluation of Bilayer Tablet of Candesartan and Hydrochlorothiazide for The Treatment of Hypertension, Journal of Drug Delivery & Therapeutics, (3), 21-35.

13. Patel H., Panchal D., 2011. Immediate type drug delivery system; A Review Journal of Pharmaceutical Science and Biopharmaceutical Research, (1), 1-20.

14. Aulton M.E., Wells T., 2002. Pharmaceutics: The Science of Dosage Form Design. Churchill Livingstone, London, UK., 500-513.

15. Parmar K., Bhatt N., 2012. An Overview Aqueous Film Coating Technology on Tablets, International Journal of Pharmaceutical and Chemical Sciences., (1), 994-1001.