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A REVIEW OF THE EMERGING TREND IN BI-LAYER TABLET TECHNOLOGY

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Abstract:

The creation of controlled release formulations with a range of characteristics to guarantee efficient drug administration is ushered in by the bi-layer tablet. By physically separating APIs, bi-layer tablets can be an effective means of preventing chemical incompatibilities and producing distinct drug release patterns. A bi-layer tablet can be used to release two medications in combination in a sequential fashion or to release a single tablet continuously, with the first layer serving as the loading dosage and the second as the maintenance dose. The next piece addresses bi-layer tablet technology, difficulties in producing bi-layer tablets, different tablet presses that are employed, quality and GMP requirements for their manufacture, different bi-layer tableting methods, and current advancements in the field of bi-layer technology.

Key Words:- *Bi-layer tablet, Incompatibility, multi-layer tablet, sustained release formulation.*

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INTRODUCTION:

For many years, oral medication administration has been recognized as the most convenient method of drug delivery. The oral method gained popularity because it is simple to administer and because it is conventional wisdom that the medicine is absorbed through the oral route just as well as through daily meal consumption. While the topical route of medication administration has been used more lately to deliver drugs to a specific portion of the body for systemic action, the parenteral route of administration is still vital in emergency situations. Since most medications have a solid physical state, solid dose forms are used to give them. The standard tablet appears to be the most widely used pharmaceutical dosage form due to its ease of transportation and relatively low production cost.[1-3]

TABLET A DOSAGE FORM: **-** The use of tablets and capsules is more prevalent in solid oral dose forms. In addition to a number of additional ingredients utilized in the creation of a comprehensive preparation, the tablets include one or more medications. "Solid preparations each containing a single dose of one or more active ingredients and obtained by compressing uniform volumes of particles" is how the European Pharmacopoeia defines tablets. Because the tablets are a tamper-proof dose form, they offer an advantage over capsules. The primary drawback of capsules compared to tablets is their increased price. If the capsules are not kept correctly, they may shatter into hard or soft capsules. Recently created, the topical method is only used for a small number of medications, such as scopolamine and nitroglycerin. Topical route has limitations in its ability to allow effective drug absorption for systemic drug action. Nevertheless, it is possible that at least 90 % of all drugs used to produce systemic effect are administered by oral route.[4,5]

FEATURES OF TABLET DOSAGE FORMS IN GENERAL: -

1. The tablet should contain the prescribed amount of the medication.
2. A regulated and consistent release of the medication from the tablet is required.
3. The tablet should have a sophisticated appearance and be devoid of flaws such as contamination, discoloration, chipping, and fractures.
4. Tablets should be strong enough to endure mechanical shocks during manufacture, packing, shipping, and dispensing.
5. They should also be chemically and physically stable enough to maintain their physical characteristics throughout time.
6. The tablet needs to be biocompatible, meaning it should not include any pollutants, excipients, or microbes that might pose a risk to patients.[6-8]

ADVANTAGES: -

1. Tablets are a unit dosage form that offers the precision of all oral dosage forms with the least amount of content variability during dosing.
2. These are the advantages of tablets as a medication delivery mechanism Of all the oral dose forms, their cost is the lowest.
3. Out of all the oral dose forms, they are the most compact.
4. When compared to other oral dose forms, they are generally less complicated to manufacture and ship.
5. Using an embossed or monogrammed punch face makes product identification easy and affordable; no further processing processes are needed.
6. They don't need a specialist and are simple to administer.
7. When compared to other unit oral forms, they are more appropriate for large-scale manufacture.
8. Their chemical, mechanical, and microbiological stability is superior. Product recognition is simple.[9,10]

DISADVANTAGES: -

1. One of the drawbacks of using tablets as a drug delivery technique is that certain pharmaceuticals are not easily compressed into dense compacts because of their low density and amorphous nature.
2. It may be challenging to synthesize or manufacture drugs with poor wetting, slow dissolving qualities, and optimal absorption high in the gastrointestinal tract as tablets that nonetheless provide acceptable or complete drug bioavailability.
3. Drugs that test bitter, have an unpleasant smell, or are oxygen-sensitive may need to be coated or encapsulated.[11-14]

BILAYER TABLET: **-** The term Bilayer tablets define as tablets which having two layers that may be either of the same drug or of two different drugs. For these types of drugs, extended-release formulations generally lead to a delayed appearance of effective plasma levels and they cannot provide a prompt

disposition of the dose immediately after administration. Bilayer tablet is suitable for sequential release of two drugs in combination, separate two incompatible substances, and also for sustained release tablet in which one layer is immediate release as initial dose and second layer is maintenance dose. Two-layer tablets may be designed for sustained release – one layer for the immediate release of the drug and second layer for extended release thus maintaining a prolonged blood level. Layers may be colored differently to identify the product.[15]

FIGURE 1 BI-LAYER TABLET

ADVANTAGES OF BILAYER TABLET:-

1. Bi-layer execution with optional single layer conversion kit.
2. Low cost compared to other dosage forms.
3. Greatest chemical and microbial stability compared to other oral dosage forms.
4. Objectionable odour and taste can be masked by coating technologies.
5. Flexible concept.
6. Offer greatest precision and the least content uniformity.
7. Easy to swallow with least hang up problems.
8. Fit for large scale production. [16-18]

COMBINATION OF TWO DRUGS:-

A) Bi-layer tablets can be designed in such a manner as to modify release as either of the layers can be kept as extended and the other as immediate release.
B) Expansion of a conventional technology.
C) Maintain physical and chemical stability.
D) Product identification is easy.
E) Easiest and cheapest to package and strip. [16-18]

MANUFACTURING OF BILAYER TABLETS: -

The simplified description of the double-layer manufacturing process can be offered as follows. that are set to apply the right amount of force for achieving the target tablet hardness. Conventional dosage form produces wide range of fluctuation in drug concentration in the blood stream and tissues with subsequent undesirable toxicity and poor efficiency. This dynamic such as repetitive dosing and erratic absorption led to the concept of controlled drug delivery systems.[19]

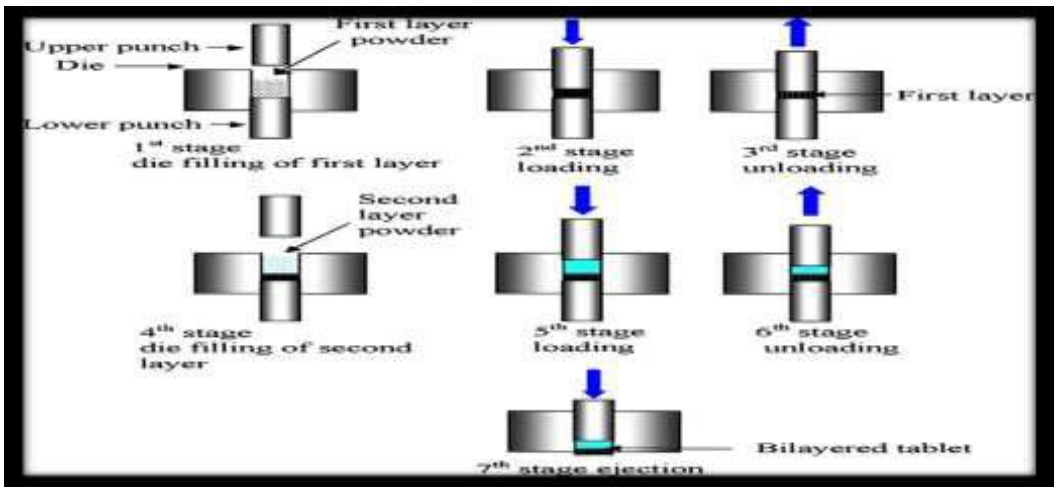

FIGURE 2:- MANUFACTURING OF BILAYER TABLETS

A- Die filling, B- compression, C- decompression, D- lower punch removal and reapplication of load to the upper punch, E-tablet fully ejected.

CRITICAL FACTORS TO BE CONSIDERED FOR BILAYER TABLET MANUFACTURING: -

The most common concerns are addressed briefly below.

A) Cross-contamination or color "bleeding"-It is imperative in virtually all cases of double-layer manufacturing to ensure that the granulations for the different layers are contained effectively by the feed frames and subsequent scraper assemblies so as to minimize or eliminate the possibility of the colors bleeding together. This is especially important in the case of an uncoated tablet that utilizes different color granulations, and can also be necessitated in cases where mixing the granulations compromise product efficacy.

B) Layer binding-A tablet press must have versatile compression force capabilities, so as to foster good binding between layers. If good binding cannot be achieved it may result in lamination of the final tablet, where the two layers separate from one another after ejection.

C) Output capabilities-The press design must effectively meld all engineering characteristics into a package that optimizes output speeds, while ensuring good final tablet characteristics for criteria such as weight, thickness and hardness.

1. First-layer sampling-This feature receives more and more attention these days, as it is critical to the overall integrity of the final product. The tablet press must have, at a minimum, the capability of periodically manufacturing layer samples, where the layers are intentionally kept separate in an effort to ensure good weights. The process must also be fast and accurate, as there is the potential for waste during the sampling interval. Novel methods for optimizing this entire process are now being made commercially available.

2."Second-layer-only" tablets-This is the typical problems observed because of the first layer sampling. A partial tablet is the result of such a sampling. To avoid this, a specifically designed discharge chute is necessary.

3.Weight control for individual layers-Early double-layer tablet presses were outfitted with weight control systems that would monitor and adjust total weight only, rather than that of the individual layers. But now systems are available which allow for greater accuracy and control in the adjustment of independent layers.

4.Compaction principles governing weight control-Unlike conventional tablets, bilayer tablets require three weight controls, namely, individual layers and the final tablet weight control. The complexity in the weight control significantly increases the level of sophistication needed in the rotary press designed for multi-layer tablets. Typically, in closed-loop control systems, two different types of control mechanisms for weight are involved.

5.Compression force-Since the material in the die cavity is compressed twice to produce a bilayer tablet, compressed first with layer one followed by both the layers, the compression force affects the interfacial interaction and adhesion between the two layers.[20-25]

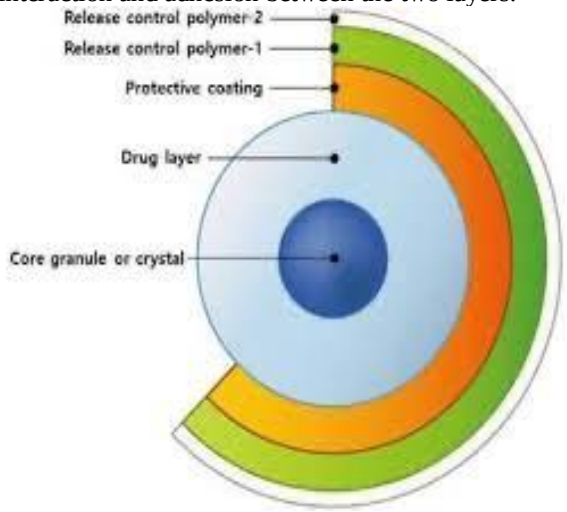

FIGURE 3:- BILAYER TECHNOLOGY

VARIOUS TECHNIQUES FOR BILAYER TABLET:-

A) OROS®pushpullTechnology:-This system consists of mainly two or three layers among which the one or more layer is essential of the drug and other layer are consist of push layer. The drug layer mainly consists of drug along with two or more different agents. So, this drug layer comprises of drug which is in poorly soluble form. There is further addition of suspending agent and osmotic agent.

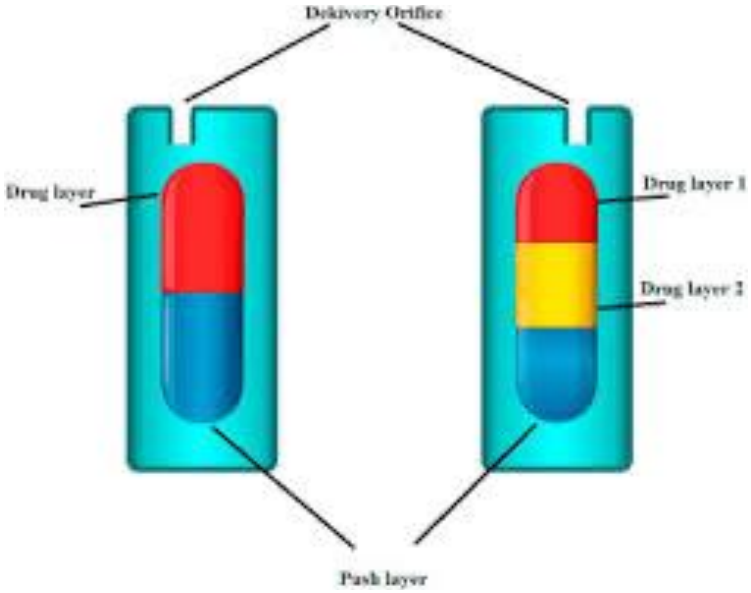

FIGURE4:- OROS®pushpullTechnology

B) L-OROS™ Technology:-This system used for the solubility issue Alza developed the L-OROS system where a lipid soft gel product containing drug in a dissolved state is initially manufactured and then coated with a barrier membrane, then osmotic push layer and then a semi permeable membrane, drilled with an exit orifice

C) ENSOTROL Technology:-Solubility enhancement of an order of magnitude or to create optimized dosage form Shire laboratory use an integrated approach to drug delivery focusing on identification and incorporation of the identified enhancer into controlled release technologies

D) DUREDASTM Technology: -This system is also known as Elan drug technologies' Dual release drug delivery system. DUREDASTM Technology is a bilayer tablet which can provide immediate or sustained release of two drugs or different release rates of the same drug in one dosage form. The tableting process can provide an immediate release granulate and a modified-release hydrophilic matrix complex as separate layers within the one tablet. The modified-release properties of the dosage form are provided by a combination of hydrophilic polymers.

E) 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 the miniature drug dispensing system that opposes like a miniature syringe and release minute quantity of concentrated form in continues and consistent from over months or year.[26-33]

LIMITATIONS: -

A) Limitations of the single sided press:-Various types of bi-layer presses have been designed over the years. The simplest design is a single-sided press with both chambers of the double feeder separated from each other. Each chamber is gravity- or forced-fed with a different powder, thus producing the two individual layers of the tablet[15,16]. When the die passes under the feeder, it is at first loaded with the first-layer powder followed by the second-layer powder. Then the entire tablet is compressed in one or two steps (two = pre- and main compression). The two layers in the die mix slightly at their interface and in most cases bond sufficiently. So that no layer- separation occurs when the tablet is produced. This is the simplest way of producing a bilayer tablet. It undergoes certain limitation as follow.

1.No weight monitoring/control of the individual Layers.

2.No distinct visual separation between the two Layers.

3.Very short first layer-dwell time due to the small compression roller, possibly resulting in poor de-aeration, capping and hardness problems.

4.Very difficult first-layer tablet sampling and sample transport to a test unit for in-line quality control and weight recalibration to eliminate these limitations, a double-sided tablet press is preferred over a single-sided press.

5. A double-sided press offers an individual fill station, pre -compression and main compression for each layer. In fact, the bi-layer tablet will go through four compression stages before being ejected from the ress.

B) Limitations of "compression force" -controlled tablet presses:-Separation of the two individual layers is the consequence of insufficient bonding between the two layers during final compression of the bi-layer tablet. Correct bonding is only obtained when the first layer is compressed at a low compression force so that this layer can still interact with the second layer during final compression of the tablet. Bonding is severely restricted if the first layer is compressed at a too-high compression force. The low compression force required when compressing the first layer unfortunately reduces the accuracy of the weight monitoring/control of the first layer in the case of tablet presses with "compression force measurement. Most double-sided tablet presses with automated production control use compression force to monitor and control tablet weight. The effective peak compression force exerted on each individual tablet or layer is measured by the control system at main-compression of that layer. There exist a typical exponential relationship between the measured peak compression force [F] and layer or tablet weight [W].This measured peak compression force [F] (under constant thickness) is the signal used by the control system to reject out-of-tolerance tablets and correct the die fill depth when required. The above graph indicates that the sensitivity δF/ δW decreases with decreasing compression force (i.e. when the distance between the compression rollers is made greater). This decreasing sensitivity is inherent to an exponential relationship and therefore inherent to the compression force- controlled system. The rate at which the sensitivity decreases depend on the formulation or powder characteristics. This is the reason why a compression force control system is always based on measurement of compression force at main-compression and not at precompression since a higher compression force is required to obtain sufficient sensitivity, thus allowing a more accurate control. A weight control system based on compression force monitoring is not the best solution for first layer weight control in a bi-layer tableting process. A compression force-controlled system requires a minimal compression force of several hundreds of daN. However, many bi-layer formulations require a first layer compression force of less than 100 daN in order to retain the ability to bond with the second layer. Above 100 daN, this ability may be lost, bonding between both layers may not be sufficient, resulting in low hardness of the bi-layer tablet and separation ofthe two layers. This basic problem, inherent to the principle of compression force monitoring is overcome by using a different weight monitoring system based upon 'displacement'.

"Displacement measurement" as the alternative to "compression force measurement" has the advantage that accuracy increases with reduced compression force. At higher production speed, the risk of separation and capping increases but can be reduced by sufficient dwell time at all four compression stages. Weight monitoring based upon 'displacement' also provides increased dwell time in addition to good bonding between the two layers, with improved and accurate weight monitoring/control of the first layer. A double-sided tablet press with "displacement measurement" is thus the preferred press to produce bi-layer tablets. This double-sided tablet press has been specifically designed and developed for the production of quality bi-layer tablets and provides:

- 'Displacement' weight monitoring/control for accurate and independent weight control of the individual layers
- Low compression force exerted on the first layer to avoid capping and separation of the two individual layers
- Increased dwell time at precompression of both first and second layer to provide sufficient hardness at maximum turret speed
- Maximum prevention of cross-contamination between the two layers
- A clear visual separation between the two layers [34-36]

VARIOUS ASPECTS OF BILAYER TABLET: - Floating Drug Delivery Systems (FDDS) From the formulation and technological point of view, the floating drug delivery systems are considerably easy and logical approach in the development of Gastro retentive dosage forms (GRDFs).

Approaches to design Floating Drug Delivery System: -

The following approaches have been used for the design of floating dosage forms of single- and multiple-unit systems.Intra gastric bilayered floating tabletsThese are also compressed tablet as shown in figure and contain two layers i.e.i. Immediate release layer ii. Sustained release layer.

Multiple unit type floating pill:-These systems consist of sustained release pills as 'seeds' surrounded by double layers. The inner layer consists of effervescent agents while the outer layer is of swellable membrane layer. When the system is immersed in dissolution medium at body temperature, it sinks at once and then forms swollen pills like balloons, which float as they have lower density. [37]

QUALITY AND GMP-REQUIREMENTS: - To produce a quality bi-layer tablet, in a validated and GMP way, it is important that the selected press is capable of:-

1.Preventing capping and separation of the two individual layers that constitute the bi-layer tablet.
2.Preventing cross-contamination between the two layers.
3. Producing a clear visual separation between the two layers.
4.High yield.
5. Accurate and individual weight control of the two layers.
6.Providing sufficient tablet hardness [38]

VARIOUS TYPES OF BILAYER TABLET PRESS:

1. Single sided tablet press

a) Limitations of single-sided press are:

1. No weight monitoring/control of the individual layers.
2. No distinct visual separation between the two layers.
3. Very short first layer-dwell time due to the small compression roller, possibly resulting in poor de-aeration, capping and hardness problems.
4. Very difficult first-layer tablet sampling and sample transport to a test unit for in-line quality control and weigh calibration.

2. Double sided tablet press: -Most double-sided tablet presses with automated production control use compression force to monitor and control tablet weight. The effective peak compression force exerted on each individual tablet or layer is measured by the control system at the main compression of the layer. This measured peak compression force is the signal used by the control system to reject out of tolerance tablets and correct the die fill depth when required.

IMMEDIATE RELEASE DOSAGE FORM:

Definition: Immediate release tablets are those which disintegrate rapidly and get dissolved to release the medicaments. Immediate release may be provided for by way of an appropriate pharmaceutically acceptable diluent or carrier, which diluent or carrier does not prolong the rate of drug release and/or absorption. Immediate release tablets are one of the tablets prepared by direct compression method. Immediate release tablets have received ever increasing demand during the last decade and the field has become a rapidly growing area in the pharmaceutical industry because of such tablets readily dissolve or disintegrate in generally less than 60 seconds. As disintegration plays a crucial role, so for development of solid orals, formulators are fascinating towards selection of proper disintegrants / super disintegrants in dosage systems. Disintegrants are substances or mixture of substances added to the drug formulations, which assist dispersion or breakup of tablets and contents of capsules into smaller particles for dissolution. Super disintegrants are those substances, which improves disintegration compared to disintegrants.

1.Biopharmaceutical Consideration: -Must that to consider Biopharmaceutical factor like metabolism and excretion.
2.Pharmacokinetics: -It is the meditation; study has done on absorption, distribution, metabolism, and excretion. After absorption, drug attains therapeutic level and therefore elicits pharmacological effect, so both rate and extend of absorption is important. In conventional dosage form there is delay in disintegration and therefore dissolution is fast. Drug distribution depends on many factors like tissue permeability, perfusion rate, binding of drug to tissue, disease state, drug interaction etc. Duration and intensity of action depends upon rate of drug removal from the body or site of action i.e. biotransformation. Decrease in liver volume, regional blood flow to liver reduces the biotransformation of drug through oxidation, reduction, and hydrolysis. Excretion by renal clearance is slowed, thus half-life of renal excreted drugs increases.
3.Pharmacodynamics: -Drug reception interaction impaired in elderly as well as in young adult due to undue Development of organ.
4.Decreased sensitivity of -adrenergic agonist and antagonist: -Decreased ability of the body to respond reflexive stimuli, cardiac output, and orthostatic hypotension may see in taking antihypertensive like prazosin. Altered response to drug therapy-elderly show diminished bronchodilator effect of theophylline shows increased sensitivity to barbiturates. Concomitant illnesses are often present in elderly, which is also taken into consideration, while multiple drug therapy prescribed. Concomitant illnesses are often present in elderly, which is also taken into consideration, while multiple drug therapy prescribed. Immunity is less and taken into consideration while administered antibiotics. Research workers have clinically evaluated drug combination for various classes‟ cardiovascular agents, diuretics, anti-hypertensive etc. for immediate release dosage forms. The combination choice depends on disease state of the patient. [39-41]

CRITERIA FOR IMMEDIATE RELEASE DRUG DELIVERY SYSTEM:

The case of solid dosage it should dissolve or disintegrate in the stomach within a short period.

1. In the case of liquid dosage form it should be compatible with taste masking.
2. Be portable without fragility concern.
3. It should not leave minimal or no residue in the mouth after oral administration.
4. Exhibit low sensitivity to environmental condition as humidity and temperature.
5. Be manufactured using conventional processing and packaging equipment at low cost.
6. Rapid dissolution and absorption of drug, which may produce rapid onset of action. [42-44]

Merits of Immediate Release Drug Delivery System:-

1. Improved compliance/added convenience.
2. Ability to provide advantages of liquid medication in the form of solid preparation.
3. Adaptable and amenable to existing processing and packaging machinery.
4. Cost-effective.
5. Improved solubility of the pharmaceutical composition.
6. Decreased disintegration and dissolution times for immediate release oral dosage forms. [45]

Challenges to Developed Immediate Release Drug Delivery System:-

1. It should dissolve or disintegrate in the stomach within a short period.
2. Be portable without fragility concern.
3. Have a pleasing mouth feel.
4. Should not leave minimal or no residue in the mouth after oral administration.
5. Should exhibit low sensitivity to environmental condition as humidity and temperature.
6. Be manufactured using conventional processing and packaging equipment at low cost.
7. Rapid dissolution and absorption of drug, which may produce rapid onset of action. [46]

SUSTAINED RELEASE DOSAGEFORM: -

Definition: A Sustained release dosage form is defined as "Any drug or dosage form modification that prolongs the therapeutic activity of the drug". Sustained release, sustained action, prolonged action controlled release, extended action, timed release, depot and repository dosage forms are terms used to identify drug delivery system that are designed to achieve or prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose.[23-26] This delivery system is increasingly being used in the treatment of acute and chronic diseases as they maintain the concentration of drug in plasma above the minimum effective concentration to and below the minimum toxic level for an extended period of time.

Disadvantages of Conventional dosage forms

1. Poor patient compliance, increased chances of missing the dose of a drug with short half-life for which
   frequent administration is necessary.
2. The unavoidable fluctuations of drug concentration may lead to under medication or overmedication.
3. A typical peak-valley plasma concentration time profile is obtained which makes attainment of steady-
   state condition difficult.
4. The fluctuations in drug levels may lead to precipitation of adverse effects especially of a drug with small
5. Therapeutic Index (TI) whenever over medication occur.

Recently, several advancements in drug delivery system have been made to overcome the drawback of conventional drug delivery system. These techniques can control the rate of drug delivery, sustaining the duration of therapeutic activity or targeting the delivery of drug to tissue.

Advantages of Sustained release dosage form: -

1. The frequency of drug administration is reduced.
2. Patient compliance can be improved.
3. Reduced 'see-saw 'fluctuation.
4. Drug administration can be made more convenient as well.
5. The blood level oscillation characteristic of multiple dosing of conventional dosage forms is reduced.
6. Better control of drug absorption can be attained, since the high blood level peaks that may be observed
   after administration of a dose of a high availability drug can be reduced.
7. The characteristic blood level variations due to multiple dosing of conventional dosage forms can be
   Reduced.

8. The total amount of drug administered can be reduced.
9. Safety margins of high potency drugs can be increased and the incidence of both local and systemic adverse
10. side effects can be reduced in sensitive patients.
11. Improve efficiency in treatment.

Disadvantage of Sustained release dosage form: -

1. Dose dumping.
2. Reduced potential for dose adjustment.
3. Cost is more than conventional tablet.
4. Increase potential for first pass metabolism.
5. Patient education is necessary for proper medication.
6. Systemic availability is decreased in comparison to immediate release conventional dosage forms.
7. Poor in vivo and in vitro correlations. [47-53]

Drug properties, which are suitable for, extended-release formulation: -

a) Physiochemical Properties of the drug:-

1. Aqueous solubility:(>0.1mg/ml)
2. Partition co-efficient: (1000:1 octanol: water system)
3. Drug stability in vivo: (High enough, so drug remain stable during release from system)
4. Protein binding: (Drug with high protein binding will not require release modification)
5. Drug pKa & ionization at physiological pH: (pKa for acidic API= 3.0 - 7.5, pKa for Basic API = 7.0 -11.0)
6. Mechanisms and sites of absorption: (Mechanism of absorption should not be active type and absorption window should not be narrow)
7. Molecular size and diffusivity: (Molecule size should be small (100-400 D so it can be easily diffused through polymer matrix)
8. Dose size:(<300mg)

b) Biological Properties of Drug:-

1. Distribution: (A.P.I. with large volume of distribution is not suitable).
2. Metabolism: (A.P.I. should be metabolized with intermediate speed).
3. Half-life of drug: (2 - 8hrs).
4. Margin of safety: (High enough so dose dumping does not cause any serious side effect).
5. Plasma concentration response relationship: (A.P.I. having linear relationship is better candidate).

Type of sustained release formulation: - Sustained (zero-order) drug release has been attempted to be achieved, by following classes of sustained drug delivery system.

Diffusion controlled sustained system: -Diffusion process shows the movement of drug molecules from a region of a higher concentration to one of lower concentration. In this system the rate controlling step is not the dissolution rate but the diffusion of dissolved drug through a polymeric barrier. The two types of diffusion-controlled system are–

1.Matrix System.
2.Reservoir System.

Dissolution sustained systems: -In these products, the rate dissolution of the drug (and thereby availability for absorption) is controlled by slowly soluble polymer or by microencapsulation. Once the coating is dissolved, the drug becomes available for dissolution. By varying the thicknesses of the coat and its composition, the release rate of drug can be controlled. A drug which having a slow dissolution rate these drugs are naturally sustained and for those drugs with high water solubility, decrease their dissolution rate through appropriate salt or derivative formation. The two types of diffusion-controlled system are –

1.Soluble matrix system.
2.Soluble reservoir system. [54-58]

EVALUATION OF SUSTAIN RELEASE BILAYER TABLET: -

1) Tablet Thickness and Size:-Thickness and diameter of tablets are important for uniformity of tablet size. Thickness and diameter is measured using venire calliper.

2) Tablet Hardness:-The resistance of tablets to shipping or breakage under conditions of storage, transportation andhandling before usage depends on its hardness. The hardness of tablet of each formulation was measured by Monsanto hardness tester. The hardness was measured in kg/cm^2.

3) Friability:-Friability is the measure of tablet strength. Friabilator is used for testing the friability using the procedure: Twenty tablets are weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min, the tablets were weighed and the percentage loss in tablet weight is determined

% loss = Initial weight of tablets – Final weight of tablets ×100 Initial weight of tablets

4) Uniformity of weight:-Twenty tablets are selected at random and the average weight is calculated. Weight Variation is calculated and is compared with I. P. standards. [59-60]

CHARACTERIZATION OF BILAYER TABLET: -

1) Particle size distribution: -The particle size distribution is measured using sieve shaker.
2) Photo-microscope Study
3)Photo-microscope images are taken(450Xmagnifications) by photomicroscope
4) Angle of Repose:- The diameter of the powder cone is measured and the angle of repose is calculated using the following equation.

Tan Ø=h/r

Where, h and r are the height and radius of the powder cone.
5) Moisture Sorption Capacity: -All disintegrates have capacity to absorb moisture from atmosphere which affects moisture sensitive drugs. Moisture sorption capacity is performed by taking 1 g of disintegrate uniformly distributed in petri-dish and kept in stability chamber at 37±1°C and 100% relative humidity for 2 days and investigated for moisture uptake by difference between weights.
6) Compressibility: -The compressibility index of the disintegrate is determined by Carr's compressibility index.

%compressibility = Tapped density – Bulk density
Tapped density

7) Stability Study (Temperature dependent):-The bilayer tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies.The tablets are withdrawn after a period of 15 days and analyzed for physical characterization (Visual defects, Hardness, Friability and Dissolution etc.) and drug content. The data obtained is fitted into first order equations to determine the kinetics of degradation. Accelerated stability data are plotted according Arrhenius equation to determine the shelf life at 25°C. [60]

CONCLUSION:

Bi-layer tablets offer an excellent opportunity for manufacturers to separate themselves from their competitors, improve their products' efficacy, and protect against impersonator products. Bi-layer tablet quality and GMP requirements can vary widely. This explains why many different types of presses are being used to produce bi-layer tablets, ranging from simple single-sided presses to highly sophisticated machines. When a quality bi-layer tablet needs to be produced in conjunction with accurate weight control of both layers, compression force-controlled presses are clearly limited because of their insufficient sensitivity and hence lack of accuracy at low compression forces required to secure interlayer bonding. Such problems become even more apparent when the tableting speed is high or increased. Accurate individual layer weight monitoring/control at high speed and in combination with reduced layer separation risk can be achieved with the displacement weight control system-based presses.

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