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RESEARCH ARTICLE

A REVIEW OF CHALLENGES AND POSSIBILITIES OF BILAYER TABLET TECHNOLOGY

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Abstract

Bilayer tablet making process involves certain challenges as well as advantages. Bilayer tablets are the prescriptions which comprise of two same or various medications consolidated in a solitary portion for viable treatment of the illness. Persistent consistence and cost measure are two significant boundaries in treatments. Bilayer tablets manage these focuses adequately. To deliver a decent quality bi-layer tablet, the apparatus should be built according to GMP. Different hardware are accessible to beat normal bi-layer issues, for example, layer detachment, lacking hardness, weight control, cross defilement between the layers and so forth. Bilayer tablets give one of the significant plan approaches where inconsistent medications, with an alternate sign, and same medication with various delivery rate can be combined in a solid unit. Bilayer tablet is reasonable for consecutive arrival of two medications in blend, and for supported delivery tablets in which one layer is promptly delivered as introductory portion and the subsequent layer is a controlled portion. Controlled delivery dose structures have been broadly used to improve treatment with a few significant medications. Utilization of bilayer tablet is an altogether different viewpoint for calming and pain relieving drugs. This review article clarifies what are the outcomes to be looked and how to be faced during bilayer tablet production.

Introduction:-

An ideal drug delivery system is such that provides the required amount of drug within a short duration and also maintains the steady level of drug concentration throughout the dosing period (Chien, 1990)[1].prepration of multilayer tablets involves exact selection of excipients and equipment parameters. Preparation of bilayer tablets was explained in fig1.

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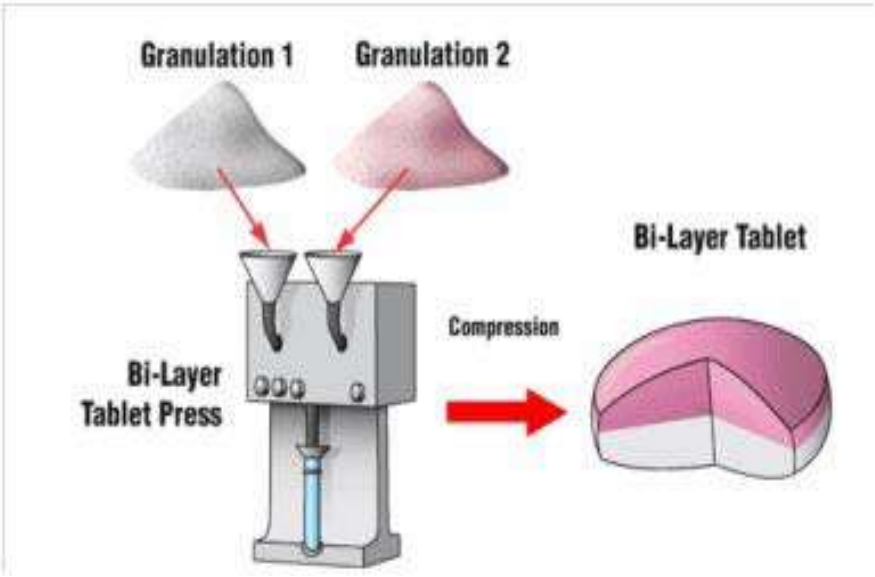

Figure 1:- Concept of preparation of bilayer tablet.

Good manufacturing requirements of bilayer tablets[2]:

To produce a top quality bi-layer tablet, during a validated and GMP-way, it's important that the chosen press is capable of preventing capping and separation of the 2 individual layers that constitute the bi-layer tablet.

1. Providing sufficient tablet hardness.
2. Preventing cross-contamination between the two layers.
3. Producing a transparent visual separation between the 2 layers.
4. High yield.
5. Accurate and individual weight control of the 2 layers.

Difficulties in bilayer tablet manufacturing[3]and their remedy:

Reasonably, bilayer tablets can be viewed as two single-layer tablets packed into one. In Practice, there are some arrangement difficulties.Diabetic, antihypertensive, antihistamines, analgesics, antipyretics, anti-allergic agents are mainly suitable for this type of drug delivery[4]. Bilayer tablets have certain key advantages and applications as compared to standard monolayer tablets[5].

Lamination

Tablet self-destructs when the two parts of the tablet don't bond totally. The two granulations ought to follow when compacted. Lamination is caused by air entrapment in granules, too much moisture or dryness, insufficient binding, improper lubricant, rapid relaxation of peripheral regimes of tablet on ejection from a dye.

Figure2:- Delamination of bilayer tablet

Remedy

Ankurchowdhary etal[6], has explained how lamination can be controlled, lamination is a major problem of all the defects in tablet manufacturing.Airentrapment can be overcome by doing a pre-compression, removing fine particles will also reduce cause of lamination. Hygroscopic substances such as sorbitol and methylcellulose are added for moisture problem. For improper binding pregelatinized starch and gum acacia is used, increasing or changing lubricant will limit lamination.

Cross-contamination

When the granulation of the primary layer mixes with the granulation of the subsequent layer or the reverse way around, cross-contamination occurs. It may vanquish the very explanation behind the bilayer tablet. Real buildup collection goes far toward hindering cross pollution. The figure4 explains how cross contamination of tablet occurs.

Figure 3:- cross contamination of tablet.

Remedy

Ensuring turret run out is less than 0.003 inch, set the feeder tablet area at a height that prevents excessive powder from reaching the turret, examine the scrapper bars, ensuring that the die fits tightly and not allowing the powder top lodge in crevices,vaccum is set as per GMP requirements, secure all vacuum hoses and ports tightly[7,8].

Yield

To forestall cross defilement, dust assortment is required which prompts misfortunes. Subsequently, bilayer tablets have lower yields than single-layer tablets. A bilayer tablet press cannot allow material to turn with turret because of contamination of other layer. So a fill cam of required size should be selected to get a product yield.

Remedy

Matt bundenthal has explained how to achieve high yields in bilayertablets.85%. Multi-layer yields can be as high as 92%, however, on a press with excellent first-layer sampling features; sampling frequency, and the time it takes to cycle through a sample, can be precisely adjusted on select presses, resulting in significantly improved yields, using triclamp fittings in hopper, feeder positioning, feed sealing, fill cam sizing, tooling tolerances, conditioning and positioning of product scrapers, penetration depths etc.

Cost

Bilayer tableting is more costly than single layer tableting for a few reasons. To start with, the tablet press costs more. Second, the press by and large runs all the more gradually in bilayer mode. Third, improvement of two viable granulations is must, which implies additional time spent on detailing improvement, investigation and approval. These elements, if not well controlled/streamlined, somehow will sway the bilayer pressure essentially and the quality qualities of the bilayer tablets (adequate mechanical solidarity to keep up its respectability and individual layer weight control). Consequently, it is basic to get an understanding into the main drivers to empower plan of a powerful item and cycle.

Remedy

Parnapalli Malathi[10]explains that usage of purpose built tablet press can be used to overcome bilayer problems, so the lesser the problems the less will be the cost. The bi-layer execution, single-layer conversion kit and exchangeable turret offer unprecedented flexibility. The XM 12 Bi-Layer Tablet Press shown in figure 4 offers a replacement standard in GMP with extreme accessibility to the compression zone and a mix of quick disconnects

and smooth surfaces that permit fast cleaning and changeover[11]. The machine features a 5 KN tamping station, 40 KN precompression station, 80 KN main compression station, and a singular structural design that eliminates vibration to the top piece and base frame. The result's an extreme reduction within the operating background level.

Figure 4:- XM-12 bilayer tablet press.

Advancement in the Field of Bilayer Tablets

By using advanced techniques, by development of predetermined release profiles of active ingredients, Incorporation of incompatible active ingredients into single dosage form use of modern equipments cost can be minimized. Following are the few recent findings[12, 13] in bilayer tablet technology.

Newbilayer tablet presses

Various new bilayer tablet presses are coming into the market with various technologies. The requirements on the security of tablet presses are increasing. As are the costs of raw materials. Feasibility, therefore, is decisive for fulfillment – especially where large batches are involved.

1. The P3030 unites flexibility, state-of-the-art technology and performance. Particularly convincing its excellent price/performance(FETTE compacting)
2. Moul-D tablet press with zero gap closed powder feeder to minimize cross contamination between layers and to minimize powder loss, patented weight control system at low compression forces (GEA Company).
3. Kambert expert bilayer tablet press for research and development of bilayer tablets. It meets current GMP standards and can use typeD7B tooling which allows the employment of the same punches used in production (Kambert).
4. Fette Compacting is the only supplier that has been producing tableting presses and tools for more than 70 years. FS12, which offers up to 40% greater output, FS19, which features a 30% longer dwell time, EU19 FS, which features a 50% longer service life(FETTE compacting).
5. Pilot 200 DL may be a double layer tablet press fully conforms to GMP with layer tablet development, fully independent weight, height, and hardness(shaktipharmatech)

Applications of bilayer tablets

1. To change complete surface area available for API layer either by sandwiching with one or two inactive layers in order to achieve swellable or erodible barriers for modified release.
2. To control the delivery rateof either single or different active pharmaceutical ingredients.Table 1 shows the delivery rates of drugs of various articles

Table 1:- Delivery rate of drugs in various research articles.

AnupamsachanN et al.,(2017)	Nitazoxanide bilayer tablets	Sodium starch glycolate was used	Controlled drug release was 95% at 12th hour.

		as superdisintegrant in immediate release layer and its maximum release was 2hours	
Pamusandhya et al.,(2014)	Glimepiride and metformin hydrochloride bilayer tablets	Sodium starch glycolate and cellulose N 50 was used in immediate release and release rate was 98.44% at 15th min	HPMC100 M was used in sustained release and release rate was 98.63% at 12th hour.
Navesh veer et al.,(2018)	Telmisartan and allopurinol bilayer tablets	For immediate release invitro dissolution is 100.7%, sodium starch glycolate was used.	HPMC was used in sustained release, 99.4% drug was released at 12th hour.

To provide synergic property
Bilayer tablet can be formulated to produce the synergistic effect of drug

To provide agonistic effect
Surendra G Gattaniel al, (2012) formulated the combination of diclofenac sodium and metoclopramide in a single tablet for the treatment of migraine. Metoclopramide enhances the absorption of diclofenac sodium.

Various approaches used in bilayer tablets[16]:
They are of three types.
1. Floating drug delivery systems
2. Polymeric drug delivery systems
3. Swelling systems

Floating drug delivery systems
These are low density systems that have sufficient buoyancy to float over the gastric contents and remain buoyant in the stomach without affecting gastric emptying rate.Floating drug delivery systems has bulkdensity less than gastric fluids.In case of bilayer tablets Sustained release layer is designed as a floating layer.

Polymers used in formulation
1. Hydrochlorides: HPMC1000, 4000, HPMC k4, k15, acrylic polymers, carbopol.
2. Inert fatty materials: Beeswax, fatty acids.
3. Effervescent agents: Sodium bicarbonate, citric acid, tartaric acid.
4. Release rate accelerants: Lactose,mannitol
5. Release rate retardants: Talc, magnesium stearate, di-calcium phosphate
6. Buoyancy increasing agents: Ethyl cellulose
7. Low density material: Polypropylene foam powder.

Polymeric bioadhesive system
The adhesion of bioadhesive drugs to mucosal membranes leads to an increase in the concentration of the drug at its site of action. There will be greater amount of drug available at target site. In bilayer tablets one layer is prepared as immediate release and other with bioadhesive property. Bioadhesive polymers are used like Gum acacia, alginic acid, carbomers, HPMC, polyvinyl alcohol, polyvinylpyrrolidine and tragacanth.

Swelling systems
These are designed to be sufficiently small on administration so as not to make ingestion of the dosage form difficult. On ingestion they rapidly swell or disintegrate or unfold to a size that precludes passage through pylorus until after drug release has progressed.

Conclusion:-

The present review is based on how bilayer tablet manufacturing involves complications although we can face the difficulties and yet how one can produce good quality tablets by following Good Manufacturing Practices. It is likewise profitable for maintained arrival of medications that to keep up plasma level of medication for delayed period inside therapeutic window, accordingly preventing the peak plasma drug levels causing poisonous impacts and lowering the wastage of medication. A complete equipmental understanding must be developed through the application of scientific and quality risk management tools to develop a useful bilayer products.

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Conflict of interest

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