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SIN-SIGHTS INTO FORMULATION TECHNOLOGIES AND DESIGN ORODISPERSIBLE TABLETS: A REVIEW

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ABSTRACT:

orodispersible drug delivery systems are extensively used to improve bioavailability and patient compliance. Over the past three decades, orodispersible tablets (ODTs) have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance, improved solubility and stability profiles. The purpose of the article is to review potential advancements of ODT technology in drug delivery applications. Various techniques employed to prepare ODTs include direct compression method, freeze drying, spray drying, tablet moulding, sublimation and mass extrusion. ODTs could be preferred choice especially with those drugs sensitive to GI and for patients under category of pediatrics, geriatrics, bedridden, postoperative and who may have difficulty in swallowing the conventional tablets and capsules.ODTs are solid dosage forms containing medicinal substances which disintegrate rapidly, usually in a matter of seconds, when placed on the tongue.ODTs render enhanced acceptability due to its patient compliance as well as improved bioavailability and stability. This article reviews recent trends undertaken to develop ODTs, new ODTs technologies, suitability of drug candidate and characterization of ODTs.

Keywords: Orodispersible tablets (ODTs), Drug selection of ODTs, Methods of preparation & Evaluation of orodispersible tablet (ODTs)

Objective:-

1. To increase patient adherence
2. To improve bioavailability
3. To increase stability
4. To examine disguise
5. To adjust hormone in blood glucose(2)(15)

Drug selection cretria:-

When selecting drug candidates for administration as ODT dosage forms :

- Drugs that require controlled or sustained release, have a short half-life and require frequent dosage, are incredibly bitter or have an unpleasant taste that cannot be masked are undesirable for ODT formulation.
- Drugs whose pharmacokinetic characteristics are markedly different from those of the same dose delivered in a conventional dosage form.
- High drug loading
- disintegrate in the mouth in a few seconds without the need for water to be swallowed.
- Patients who concurrently take anticholinergic medications may not be the best candidates for these drugs
- Be compatible with taste masking and other excipients.(16)

Methods used for preparation of ODTs:-

- Melt granulation
- Effervescent method
- Cotton candy process
- Direct compression
- Tablet molding
- Sublimation
- Freeze drying

- Melt granulation :-
  Pharmaceutical powders are efficiently agglomerated using the melt granulation technique using a melt able binder. The fact that this method does not require organic solvents or water makes it superior to conventional granulation methods.
  The procedure takes less time and uses less energy than wet granulation because there is no drying step. It is a practical method to speed up the dissolving of medications like griseofulvin that are poorly water-soluble. This method involves using a hydrophilic waxy binder to make ODT with adequate mechanical integrity.(1)

- Effervescence Method :-
  Sodium bicarbonate, tartaric acid, or citric acid at a concentration of 12% (w/w) are also combined with super disintegrants including pregelatinized starch, sodium starch glycolate, crospovidone, and croscarmellose to create rodispersible tablets using the effervescent method. To start, the motor was properly combined after sodium bicarbonate and tartaric acid were preheated at a temperature of 80°c to eliminate absorbed/residual moisture. The blends are finally squeezed in the punch.(3)

- Cotton candy process:-
  In this procedure, receivers are combined with either the medications alone or with other substances to create a matrix known as FLOSS using shear form technology. The floss has a fibrous texture comparable to cotton candy fibres. At temperatures ranging from 180 to 260 degrees Fahrenheit, saccharides including sucrose, dextrose, lactose, and fructose are frequently used to make floss. At temperatures between 30 and 40% lower, other polysaccharides including polymaltodextrins and polydextrose can be transformed into fibres.(1)(3)

- Direct compression :-
  The simplest and most economical method of producing tablets is direct compression. Due to the accessibility of improved excipients, primarily super disintegrants and sugar-based excipients, this method can now be used in ODT research.(5)

- Tablet molding :-
Solid dispersions are the end product when moulding tablets. The drug's physical form in the tablet relies on whether and how much it dissolves in the molten carrier. The drug may be present in the matrix as discrete small particles or micro particles. It can either completely dissolve in the molten carrier to generate a solid solution or partially dissolve in the molten carrier with the remaining particles remaining insoluble and dispersed in the matrix. The type of dispersion or dissolution will affect disintegration time, drug dissolution rate, and mouth feel.

- Sublimation :-
For orodispersible tablets, the presence of a pore structure in the tablet matrix is essential for quick disintegration. Due to the poor porosity of the matrix, conventional compressed tablets with highly water-soluble ingredients sometimes fail to dissolve quickly. Therefore, volatile components are used to create porous matrix, which are then subjected to a sublimation process. Water can transition directly from the solid to the liquid state through a process known as sublimation. In this procedure, inert volatile ingredients like urea, urethane, naphthalene, camphor, and menthol are added to other excipients before the blend is compressed into tablets.

- Freeze drying :-
Water is extracted from the product after it has been frozen by a process called freeze drying. By using this method, an amorphous porous structure that can quickly dissolve or scatter is produced. This article covers a typical process used in the formulation of ODT when utilising this technique. A carrier or polymer is dissolved or disseminated in an aqueous solution together with the active medication component. The mixture is added by weight to the premade blister packs' walls. In order to freeze the medication solution or drug dispersion, the trays containing the blister packs are moved through a tunnel of liquid nitrogen. The freeze-drying procedure is then carried out on the frozen blister packages by placing them in refrigerator cabinets. On a blister-sealing machine, the aluminium foil backing is placed after freeze-drying.(1)

Mechanism Action of Disintegrates:

- By Capillary Action:
Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug /excipients and on tableting conditions.(1)(19)

- Air Expansion:
Whenever exothermic disintegrates are wetted, localised stress is produced as a result of capillary air expansion, which aids in tablet disintegration. This hypothesis, however, is restricted to a small number of disintegrates and is unable to explain how the majority of modern disintegration agents work.

- Enzymatic Reaction:
These enzymes assist in disintegration by destroying the binding effect of the binder.It actually causes a pill to burst due to swelling, pressure applied in an outward or radial direction, or the increased absorption of water, which results in an immense. Increase in granule volume to promote disintegration(8)

- To Deformation:
According to Hess' research, when tablet compression occurs, disintegrating particles become deformed. These deformed particles then revert to their original shape when they come into touch with aqueous material or water. There have been instances where starch's ability to expand was enhanced when its granules underwent significant deformation during compression.(3)

- Swelling:
  One of the general mechanisms of action for tablet disintegration that may be the most generally acknowledged is swelling.High porosity tablets have poor breakdown because there is insufficient swelling force. On the other hand, the tablet with poor porosity experiences enough swelling force. It is important to remember that if the packing percentage is excessively high, fluid cannot enter the tablet and disintegration occurs once more.(20)

- By Gases Released:
  When tablets are wet, carbon dioxide is released from them as a result of bicarbonate and carbonate reacting with citric acid or tartaric acid. The tablet breaks down as a result of internal pressure buildup. When a pharmacist has to create very quickly dissolving tablets or fast disintegrating tablets, they utilise this effervescent combination. Due to the disintegrants' great sensitivity to even little variations in temperature and humidity, careful environmental control is necessary for producing the tablets.(17)

- Particle/Particle Repulsive Forces:
  Another disintegration mechanism makes an attempt to explain why a tablet formed with "non-swellable" Disintegrates swells. Particle/Particle Repulsive Forces Based on the finding that nonswelling particles also contribute to tablet disintegration, Guyot Hermann put out the particle repulsion theory. The mechanism of disintegration is the electric repulsive interactions between particles, and water is necessary for it. Researchers discovered that wicking comes second to repulsion.(1)(2)

Evaluation of orodispersible tablet (ODTs):-

Precompression parameter Evaluation:-

The powder mixture's various flow characteristics such as:-
Angle of repose :-
Bulk and tapped density:-
Hausner's ratio:-
Carr's index:-

Angle of repose :-
fixed funnel method was used to determine the powder's angle of repose. A funnel was filled with the powder mixture that had been exactly weighed. The funnel's height was kept at a level where the funnel's tip barely touched the top of the powder heap. Without encountering any resistance, the powder was allowed to pass through the funnel and onto the surface. The powder cone's height and diameter were measured. The following equation was used to calculate the angle of repose:tan = h/r(2)

Bulk and tapped density:-
Each formula's 5 g of powder was added to a 25 mL measuring cylinder. To remove any possible agglomerates, it was first lightly shaken. The initial volume was recorded, then at 2-second intervals, the cylinder was allowed to drop from a height of 2.5 cm onto a hard surface under its own weight. Up till a constant volume was noticed, tapping was continued. The following formulas were used to determine the loose bulk density (LBD) and tapped bulk density (TBD) of :

LBD = powder weight /packing volume.
TBD = Powder weight/tapped volume.(1)

- Hausner's ratio:-

A good flow is indicated by a Hausner ratio
Hausner's ratio = Tapped density/Bulk density

- Carr's index:-

For a solid's ability to be compressed into a powder, the Carr Index is calculated using true density (T) and bulk density (B).

C = True density(TD) - Bulk density (BD) / True density(TD) X 100

Postcompression Evaluation (tablet evalution) :-

- Tablet Hardness
- Tablet thickness
- Weight variation
- Friability
- Drug content
- In vitro disintegration time
- In vitro dissolution
- Drug–excipient interaction study
- Stability studies

- Tablet Hardness :- A major factor in preventing tablet breakage during handling, storage, and transportation is hardness. The Monsanto hardness tester was used to measure the tablet's hardness.was measured in kg/cm2 units.

- Tablet thickness :-The thickness of the tablet was measured by positioning it between the Vernier caliper's two arms.

- Weight variation :- Twenty randomly chosen tablets from each formulation were weighed one at a time with a digital balance.The individual weights were recorded and the weight variation was determined by comparing them to the average weight(1).

- Friability :- A plastic chamber friabilator USP type Roche friabilator (Pharmalab, Ahmedabad, India) attached to a motor rotating at a speed of 25 rpm for 4 minutes received 20 tablets after being weighed. Friability = [(Initial weight Final weight)/(Initial weight)] 100%, was used to compute the percentage weight loss (friability) after the tablets were reweighed.(18)

- Drug content:- A amount of powder equal to 40mg of valsartan was placed into a 100-mL volumetric flask after ten tablets were weighed and crushed into a fine powder. The powder was then extracted using a pH 6.8 phosphate buffer. The resulting solution was filtered, and the filtrate was appropriately diluted with phosphate buffer at pH 6.8. By measuring the absorbance at 250 nm using a UV-Visible Spectrophotometer (UV-1800 with UV-Probe Version 2.34 software, Shimadzu Corporation, Japan), the amount of valsartan was found out With the use of the standard calibration curve, the drug content was calculated. 32 The average of three determinations was used to establish the mean percent drug content.

- In vitro disintegration time :- The disintegration time for each formulation was calculated using the tablet disintegration test device. Each tube of the testing device for tablet disintegration included six tablets individually. The time taken for the full pill to completely dissolve was observed, and the medium was kept at a temperature of 37 ± 2 ◦C.

- In vitro dissolution :-The study made use of a paddle-style USP type 2 dissolution test device (Electrolab TDT - 08 L Dissolution testers USP).First, 900 mL of phosphate buffer with a pH of 6.8 was poured into a jar and heated to 37 0.5 °C. The paddle rotated at a constant pace of 50 rpm. At intervals of two minutes, dissolution samples were taken, and the amount of medication was measured by measuring the absorbance at 250 nm. 34 From the standard calibration curve, the drug concentration was determined and represented as the cumulative percent of the drug dissolved.A typical tablet formulation underwent a comparable in vitro dissolving testing.(2)(1)

- Drug–excipient interaction study :- By using Fourier transform infrared spectroscopy, the compatibility of the pure drug, mixing of the drug with polysaccharide (1:1), and optimum formulations (combination of the drug with several excipients used in the creation of ODT formulation) was assessed. The KBr disc technique was used to produce the samples' IR spectra, and the scanning range was 500-4000 cm-1.

- Stability studies :- According to the ICH (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) standards, the stability study of the tablets was conducted by keeping the samples in the stability chamber at 40 20 C/75 5% RH for 3 months. Stability research was done on the optimised batch. After a one-month break, the tablets underwent evaluations for hardness, friability, drug content (Assay), disintegration time, and in vitro drug release profile.(11)

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