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A Review on Pharmaceutical Mini-Tablets

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Abstract: ***The objective of controlled drug delivery systems is to deliver the drug over an extended period of time or at a specific duration during the treatment. Oral controlled release drug delivery systems are available as single unit dosage forms (SUDFs) or multiple unit dosage forms (MUDFs).Multiple unit dosage forms are based on subunits such as pellets, granules, or minitablets. Among all MUDFs, mini tablets represent a new trend in solid dosage form design, with the main aim of overcoming drug-excipients or drug-drug interactions. They also offer an alternative for pellets and granules because of their relative ease of manufacturing and dosage forms of equal dimensions, weight with smooth regular surface can be produced in a reproducible and continuous way. They do not require for any solvent for their production as a result problems with stability can be avoided, they also require less coating material and also there is a great flexibility in formulation development. This review is focus on various aspects of mini tablets.***

Keywords: SUDFs, MUDFs, pellets, granules, Mini tablets

1. Introduction

Oral drug delivery system is most popular and convenient route of administration among all drug delivery routes. The oral medicine is commonly considered as the principal scene examined in the revelation and advancement of pharmaceutical plans and new medication elements, primarily as a result of patient convenience and acceptance in administration, and practical assembling process. For some medication substances, conventional immediate-release formulations give clinically compelling treatment while keeping up the required equilibrium of pharmacokinetic and pharmacodynamic profiles with an acceptable dimension of security to the patient. For controlled-release systems, the oral course of administration has gotten the most consideration. The aim of any dosage form is to maintain therapeutic amount of drug to the specific site by providing loading dose and maintenance dose.

Oral controlled release drug delivery frameworks can be ordered in two classifications: a. Single Unit Dosage Forms (SUDFs) - capsules, tablets; b. Multiple Unit Dosage Forms (MUDFs) - mini tablets, granules and pellets[1].

MUDFs concept was introduced in the year 1950. Multiple unit dosage forms consisting of small discrete units, with desired characteristics. MUDFs control the arrival of a drug, as appeared by the reproducibility of the medication release profiles when related to the ones acquired with SUDFs. These MUDFs are portrayed by the way that the dose is regulated as various subunits, each single unit holding the drug. The general dose is then, the total of the amount of the drug in each subunit, and the usefulness of the whole dose is legitimately identified with the usefulness of the individual subunits. The idea of MUDFs is beneficial when the chosen operators have diverse mechanism of action that give synergistic or addictive impact, diminishing the required dose as contrasted to SUDFs. After disintegration, various units gets discharged into the stomach and spread along the gastrointestinal tract bringing about reliable drug release with decreased danger of nearby disturbance. MUDFs with several mini tablets filled in to hard gelatin capsule or compacted as bigger tablets, after disintegration it release sub units as multiple dose forms. MUDFs typically consume an additional consistent in-vivo dissolution profile when contrasted to SUDFs, bringing about progressively uniform bioavailability. MUDFs have several advantages over conventional monolithic dosage forms. MUDFs may appear to be costlier than SUDFs in the tiny span; however due to, decrease being developed of opposition, additional foreseeable gastric emptying, lesser treatment disappointment rate and higher colonic residence time, results in huge investment funds[2].

2. Mini Tablets

Mini tablets are plane or slightly bended tablets with diameter extending between 3-6 mm or littler than that and have a wide application zone. For effortlessness of use, they are frequently packed in capsules, they can be compressed in bigger tablets or occupied into sachets after disintegration, discharge these subunits as various unit dosage forms. Mini tablets are formed with multiple punches using peculiar or rotary tablet press machines. Mini-tablets are great substitutes for granules and pellets since they can be easily produced and converted into controlled drug delivery system. So the advancement of mini-tablets for controlling drug release is a significant focus point of investigation into oral controlled release solid dosage systems[3].

Figure 1: Mini tablets

2.1 Advantages

- Mini tablets can be produced extensively and effectively.
- They have outstanding size uniformity, smooth surface, customized shape.
- Mini tablets offer simple preparation, identical measurements like size and weight, smooth surface and all physical parameters are reproducible in a constant way compared to pellets and granules.
- Mini tablets have high medication stacking limit.

- Strength issues are diminished because of mini tablets did not require any solvents for their generation.
- Changes from batch to batch are minimum compared to other MUDFs.
- Any drug or excipient which is difficult to coat with polymeric layer for modified drug release was adjusted as mini tablets[4].

2.2 Components of Mini Tablets

Diverse mini-tablets can be planned and framed separately, assimilated into a capsule to release the drug at specific amounts and at specific locations. Different arrangements of mini-tablets consist of delayed release, controlled release and immediate release formulations. Likewise, integrating specific mini-tablets jointly, unsuited drugs can be directed. This, as an effect, similarly associated illnesses can be preserved effectually expands whole therapeutic consequence[5].

2.3 Release outline

Increase in surface area of contact to solvent, increases the solubility leads to increase in drug release additionally using mini tablets. The release rate of the medication can be managed with prominent assurance due to put in identical level of a delaying film coat. Moreover, mini-tablets that are framed utilizing varying concentrations of HPMC K 100 M, contributes an extended drug release rates. The drug enclosed in the mini-tablets acquire released at specific rates, based upon system of mini tablets. Established on the release kinetic considerations varied, it can be determined that mini-tablets holding HPMC K 100 M are predominantly fit to release the medication over hours of time phases. By uniting separate doses of mini tablets, it is viable to accomplish several releases with one formulation. Due to substantial lesser measurements of the mini tablets, when associated to regular tablets, they move over the stomach at a faster level rate. As an outcome, the concentration of the medication in the blood can be simply reproduced[6].

2.4 Viewpoint

Mini-tablets are best suitable dosage forms for pediatrics which can be produced easily by pharmaceutical industry. Mini-tablets can be measured as a probable new formulation for pediatric usage, as they chance the desires of child-friendly drug delivery. In pediatric utilize, mini-tablets propose numerous benefits such as, the delivery of a precise dose and the chance of dose flexibility by administering multiple mini-tablets[6].

3. Categories of Mini Tablets

In view of the target site, patient needs and technique of manufacturing are classified into following categories: a. pH responsive mini tablets b. Gastro retentive min tablets c. Pediatric mini tablets d. Bio-adhesive mini tablets[1]e. Oral disintegrating mini tablets

a. pH responsive mini tablets: The pH of Gastro Intestinal Tract changes enormously for example Stomach pH 1.5-3, upper portion of small intestine duodenum 4.0-5.0, lower portions of small intestine jejunum and ileum 6.5-7.5, and colon 5.6-6.9. pH responsive drug discharge is vital when absorption of drug is additional at a specific site this can be accomplished by coating with pH sensitive polymers like Eudragits.

b. Gastro retentive mini tablets or Floating Mini Tablets: Gastro retentive mini tablets are expected to release the drug in stomach for delayed time. Commonly for tablets to float on the GI liquids content we formulate tablets by utilizing gas producing agents in them. These tablets as soon as interacted with the stomach fluids they produced gas and food create CO_2 is caught in swellable hydrocolloid which makes the tablet to float and hold in stomach. In typical single unit tablets drug stacking is low as the polymer utilized for floating in high. In mini tablets we can utilize coating with gas producing agents, for example, calcium carbonate and sodium carbonate, eudragits coating instead of swellable polymers utilized in formulation to build the drug loading. Fluid bed processor can be utilized for coating of mini tablets.

c. Pediatric Mini Tablets: In children, Tablets, capsules and syrups are regularly utilized. In there should arise an occurrence of tablets as they are challenges in dose adjustment, large in size difficulty in swallowing. Some time we need to break the tablets and control which causes loss of movement of the tablets. Patient compliance is additional problem with the conventional dosage forms. Syrups are fluid dosage forms which are easy to administer and dose can be effectively transformed to the patient needs on the further side disadvantages with these fluids dosage forms are taste issues, microbial, chemical and physical instability, and lack of controlled release and formulation issues. To overcome entire the above concerns formulating mini tablets can outcome in good patient acceptance. Mini tablets are definitely accepted by children than other dosage forms like capsules, tablets, and syrups etc.

d. Bio adhesive Vaginal Mini Tablets: Ointments, tablets, gels and creams are accessible dosage forms intended for vaginal drug delivery. The difficulties with these are messy, leakage, less retention time and less patient compliance. Nano pharmaceuticals can be utilized but the issue related with them is short residence period as they are fluid in nature. Bio adhesive polymers are utilized for avoid the above complications. Bio adhesive polymers are adhesive on contact to moisture and outwardly soluble and will promptly adhere to surfaces at low concentrations but they have high viscosity. Solid dosage forms have great dose accuracy than semisolids systems. The issue in solid dosage forms is vaginal breakdown is slow then they are promptly cleared due to self -cleansing action and attractive force of vagina. Bio adhesive polymers can be utilized to avoid this but in huge size tablets loss is reported. Bio adhesive mini tablets can be utilized for vaginal drug delivery for extended period of time and to supply drug exactly. In mini tablets dose is distributed into multiple units which will expand uniformly in vaginal cavity with upgraded coverage in vaginal epithelium. Bio adhesive Mini tablets act by establishing and swelling micro gels and discharging drug in controlled discharge way and there by extreme bioavailability can be accomplished.

e. Oral disintegrating Mini Tablets: Oral Dispersible Tablets (ODTs) are the unique dosage form which promptly disintegrates in the mouth i.e., 1-3 minutes without the required of water, chewing upon oral administration and dissimilar other conventional oral solid dosage form. ODTs are also known as bite-dispersible, mouth-dissolve, rapidly disintegrating, fast dissolve, crunch-melt, quick-dissolve, and oral dispersible tablets. ODTs are additional proper for pediatric patients since pleasant mouth feel, fast disintegration in mouth and their lesser size. The ODTs must have the following characters they must disintegrate in the mouth without additional water. The disintegrated tablet ought to turn into a fluid suspension or soft paste which can give smooth swallowing and great mouth feel. Because ODTs break down or deteriorate in the patient's mouth, the drug will be mostly dissolved in nearness to the taste buds. A pleasant taste inside the mouth ends up basic for patient acceptance. Unless the drug is tasteless or does not have an unwanted taste, taste-masking methods ought to be utilized. The taste-masking innovation should likewise be perfect with ODTs formulations[7].

4. Conceivable outcomes for formulating the mini-tablets dosage forms

4.1 Compressed Mini Tablets Systems

There has been an expanding concern for the advancement of MUDFs incorporated into tablets rather than hard gelatin capsules, in request to defeat the higher fabrication expenses of capsules. For the reason that efficient shape, their size consistency, little porosity, high achievable strength, smooth surface and mini-tablets can keep up their shape and structure in a more reproducible manner than expected granules or pellets, once they have been packed into a tablet framework. It can be estimated that when surface coarseness and shape abnormality of the mini-particles, such as granules and pellets increases, the compression performance alterations towards a progressively complex procedure that, other than densification and deformation, includes additionally attrition and fragmentation of the subunits. Biphasic release system is utilized predominantly when extreme relief desires to be accomplished rapidly, and it is followed by a sustained release stage to keep away from repeated administration. Antihypertensive, Non-steroidal anti-inflammatory drugs and anti-allergic agents, Antihistaminic are appropriate drugs for this category of administration. The pharmacokinetic benefit depend on the element that drug discharge from fast releasing constituent leads to a unexpected increase in the blood. But, the blood level is kept up at steady state as the medication is discharged from the sustaining mini-tablets[8].

Advantages

It is easy and low-cost. It is utilized to distinct incompatible ingredients. It may be utilized to generate modified release products. It is not dangerous to nature meanwhile it does not require the utilization of high measures of organic solvents[4].

4.2 Encapsulated Coated Mini Tablets Systems

Coated oral sustained-release systems of medications are generally utilized to extend the drug release and achieve targeted drug delivery. In particular, it has demonstrated challenging to create one dosage form with immediate and sustained release properties. A multiple unit and multifunctional system, which holds flexible mini-tablets in a HPMC or hard gelatin capsule, can be established by formulating Sustained Release Mini Tablets (SRMTs), Pulsatile Mini Tablets (PMTs), Immediate Release Mini Tablets (IRMTs) and Delayed Onset Sustained Release Mini Tablets (DOSRMTs), each through several lag times of discharge. Based on the combinations of mini-tablets, drug delivery systems are categorized into following categories such as site-specific drug delivery systems (DDS), zero-order DDS, slow/quick DDS, multiplied pulsatile DDS. Consideration of IRMTs licenses the improvement of quick acting encapsulated dosage forms with ideal pharmacokinetic profiles for quick action. The size of the tablet can be diminished such an extent that it could be enclosed in a capsule, then deploy tablets with various release properties within one capsule. Numerous mini-tablets can be incorporated into each HPMC capsule, which further disintegrates and discharges these subunits. Since numerous mini-tablets can be incorporated into each capsule, tablets with dose, drug release rates and dissimilar combination of drugs can be incorporated. Therefore, patient compliance can be enhanced[8].

Advantages: It causes lower treatment failure rate, huge savings. Broad therapeutic applications can be accomplished. This offers both multi-phase and controlled release for combination or single prescription and over the counter medicines. Sustained, delayed or pulsed release profiles can be accomplished. Drug delivery can be targeted to two dissimilar regions of the GI tract. It has more predictable gastric emptying, higher colonic residence time and subsequently less money required for the development of new products in long-term therapy. Delivering of incompatible drugs is also possible. Cost effective therapy and patient compliance can be accomplished[4].

4.2.1 Ideologies of Tablet Coating

The coat a tablet is regularly founded on in any event one of the convoying with goals: To control the release of the drug from the tablet. To cover the odor, color, taste of the drug. Utilize acid resistant enteric coating, to shield the drug from the gastric condition of the stomach. This is to offer chemical and physical protection for drug. Use of contrasting printing and unusual colors, expand the pharmaceutical elegance.

4.2.2 Tablet coating procedures

In most cases, the coating procedure is the last basic phase in the tablet production cycle. The effective utilization of the coating solution formula to a tablet gives the visual credentials to the product; thus the quality of the product might be made a decision on this last production stage. The kind of process preferred relies upon the type of coating that is to be applied the roughness of the tablet core, and the financial aspects of the procedure. Three kinds of tablet coatings are utilized in the pharmaceutical industry such as Film coating, Compression coating, Sugar coating.

The encapsulated coated mini tablets systems, we intended to decrease the size of the tablet such an extent that it could be enclosed in a capsule, and then deploy tablets with various

release properties inside the one encapsulated mini tablet systems. Encapsulated mini tablet systems include sustained release mini tablets (SRMTs) and immediate release mini tablets (IRMTs) in a capsule made from HPMC. Various mini tablets can be positioned into each HPMC capsule, which further disintegrates and release these subunits. Since several mini tablets can be positioned into each capsule, tablets with dissimilar content, dose and discharge features can be incorporated. Insertion of IRMTs allows the development of quick acting encapsulated mini tablet dosage forms with ideal pharmacokinetic profiles for rapid action. Encapsulated mini tablet systems can be used to yield several sustained release profiles by uniting dissimilar kinds, quantities of mini tablets and can contain combinations of dissimilar drugs, thereby improving patient compliance.

This idea of drug release might be adjusted at the core level by utilizing diverse release retardant polymers and further changed by coating the mini tablets like multiparticulate. Mini tablets are coated in modified coating pans and in fluid bed process. To ensure the IRMTs accommodated low substituted disintegrate such as hydroxy propyl cellulose, and were developed by coating mini tablets with HPMC. HPMC is a non-toxic, non- ionic, water-soluble substance that is easy to handle, comparatively easy to manufacture. In contrast, the SRMTs were coated with a mixture of HPMC and Ethyl cellulose. ETHOCEL (ethyl cellulose) products have for quite some time been utilized as a solvent-based tablet coating. Ethocel resins form strong films with great adhesion. Since ethyl cellulose is water insoluble, it is frequently utilized in conjunction with other water and organic-solvent soluble polymers, for example, Methocel cellulose ethers. Sustained release coatings can be accomplished by changing the proportions of Methocel and Ethocel cellulose ether products[9].

4.3 Compressed mini tablets systems are presented as a biphasic delivery system

Biphasic delivery systems are intended to discharge a drug at two dissimilar rates or in two dissimilar periods of time, i.e., slow/quick or quick/slow. A quick/slow discharge approach delivers a preliminary burst of medication discharge followed by a constant rate of discharge over a well-defined period of time and in slow/quick discharge approach delivers vice versa. Biphasic discharge framework is utilized predominantly when most effective therapeutic dose needed, and it is followed by a sustained release period to escape repeated administration. Antihypertensive, anti-allergic agents, antihistaminic, non-steroidal anti-inflammatory drugs are utilized for this kind of administration. Usually, conventional controlled dosage forms do not give a quick onset of action and delay the discharge of therapeutic systemic levels. Although immediate release granules provide quick release to give quick onset of action, then fails to give extended period of action. A moderately constant plasma level of a medication is frequently desired to keep up the drug concentration within the therapeutic window. However, it is hard to attain, particularly for once-daily dosage forms, partially since the environment for medication absorption or diffusion differs along the gastrointestinal tract. On the basis of these considerations, we have suggested a novel oral delivery device, in the form of a double-component granules and tablets, in which the one portion is framed to get a rapid discharge of the medication, with the purpose of getting a high serum concentration in a small period of time. The second portion is a sustain discharge matrix, which is outlined to keep up a virtual plasma level for an extended period of time[10].

5. Manufacturing Methods for Mini Tablets[11]

A portion of techniques that can be utilized for the manufacturing of mini tablets are: A. Direct compression, B. Dry granulation, C. Wet granulation, D. Melt- extrusion.

A. Direct Compression Method: In direct compression method, powder blends containing excipients and active pharmaceutical ingredients are directly compressed the powder blends into mini tablets. Hardness is depending on the excipients direct compression grade. A powdered blend flow into a die, the upper and lower punches of the tablet machine compress, the material under a high pressure to produce a mini tablets. In this process, powder blend containing Active pharmaceutical ingredient, excipients, lubricants followed by compression, which makes the product simple and easier process, no other additional processing steps are required. Direct compression method is most commonly used because it requires less time, most effective and least complex way to produce mini tablets. Stability problems are lower compared to wet granulation method.

B. Dry Granulation Method: Dry granulation method is a logical approach for the manufacturing mini tablets. In these method granules are formed by slugging. Thermo labile and moisture sensitive drugs are suitable for manufacturing mini tablets by this method. Roller compactor is used as processing equipment in this method. In this method premixed powders between two counter rotating rollers under extreme pressure, mini tablets are compressed.

C. Wet Granulation Method: In wet granulation method active ingredient, diluents, disintegrates are well mixed to form granules, which are further compressed in compression machine to produce mini tablets. In this method, binding agents are different grades of polyvinyl pyrrolidine are used.

D. Melt-Extrusion Technique: In Melt-Extrusion Technique, the powder (Drug + excipients) were premixed this premixed powder is then moved to dissolve extruder. In melt-extruder parameters like temperature, screw speed and feed rate are set in the scope of melting point scope of material. After the procedure extrudes are then processed and sieved. The acquired granules are then compressed to mini tablets utilizing compression machine.

5.1 Formulation of Mini Tablet in Capsule Systems:

The formulation development of Mini Tablet in Capsule Systems can be classified into three essential stages:

- The formulation/production of mini-tablets,
- Coating of these mini tablets with appropriate coating polymer,
- Filling of coated mini tablets into HPMC or hard gelatin capsules[6].

Formula utilized for the calculation of immediate release dose:[12]The pharmacokinetic considerations of drug were utilized for the calculation of theoretical drug release outline for coated mini tablets in capsule system. The immediate release portion of drug was calculated utilizing the following equation.

$$DL = C_{max} X V_d$$

Where DL = Loading dose, C_{max} = maximum plasma concentration, V_d = volume of distribution.

Preparation of immediate release constituent (Granules): Calculated quantity of immediate release dose medication and additional appropriate excipients (Microcrystalline cellulose) were utilized since of its good disintegration and compaction properties. Super disintegrants were utilized to acquire an immediate release of the drug. The wet granulation method is utilized for the preparation of granules.

Preparation of Immediate Release Coated Mini Tablet (IRCMT)[13]: The IRCMT was prepared utilizing the wet granulation method. The ingredients containing of intended quantity of immediate release dose drug, further excipients (anhydrous dibasic calcium phosphate, hydroxyl propyl cellulose, D-mannitol) and superdisintegrants in quantities varying according to the experimental strategy were passed through 60 number mesh individually and dry mixed. The dry mixing was conducted for 10 min and the blend was granulated with ethanol. The resulting wet mass was instantly passed through 16 no. mesh screen. The granules acquired were dried for 1 hour in a thermostatic hot air oven maintained at 30-35^{0}C. The lubricated granules were compressed into mini-tablets in a rotary tablet press. The mini-tablets were coated with an aqueous ethanolic solution of HPMC utilizing a pan coating system to yield a 5 % increase in weight. Percentage weight gain calculated by following equation:

$$\text{Percentage weight gain} = [(Wt - Wo)/Wo]X100$$

Where, Wt = Weight of tablet after coating, Wo= Initial weight of tablet.

Preparation of Sustained Release Coated Mini Tablet (SRCMT)[13]: The SRCMT was prepared utilizing the similar method as utilized for preparing the IRCMT. However, the SRCMT did not contain disintegrants. Ethyl cellulose, HPMC, ethylalcohol, Magnesium stearates and water utilized for preparation of coating suspension. To reduce friction between the surfaces of mini- tablets since utilizing magnesium stearate in the coating preparation, the mini-tablets-filling system and the HPMC capsules.

Preparation of Coated Mini Tablet in Capsule System (CMTICS)[14]: Varying number of IRCMT and SRCMT were positioned in each HPMC capsule (size1) in the preparation of CMTICS. Both diverse/similar proportions of sustained release coated mini tablets were positioned in each HPMC capsule to accomplish several sustained release profiles of the CMTICS.

5.2 Mini tablets to be administer by subsequent methods:

5.2.1 Directly administered as single units: Mini tablets can be directly administered as such. Requisite dose can be simply taken and these are filled in bottles. Previous compressed mini tablets are additional compressed to acquire tablets of usual size.

5.2.2 Filled in hard gelatin capsules: As it is hard to handle the mini tablets these are typically filled in hard gelatin capsules and then administered[15].

5.2.3 Automatic dose dispensing device: Based on the patient population average dose individualization, dose should be decided is significant as administration of correct medication in wrong dose will outcome in adverse effects of reduced efficiency. Usually tablets are generally utilized however partial strengths available for administration. Separating tablets for receiving vital dose or combining dissimilar strengths will not provide the preferred therapeutic effect so an automatic dose dispensing device can be utilized to distribute tablets of necessary dose.

6. Evaluation of Mini Tablets

6.1 Pre formulation studies for Mini Tablets[16]:

Pre-formulation studies describe physical and analytical profiles to develop stable pharmaceutical dosage form. Describes Flow properties: Angle of repose, Bulk density, Tapped density, Compressibility index, Hauser's ratio and Drug-excipient compatibility studies: FTIR, DSC.

i. Angle of repose: Weighed amount of powder mix was taken, allowed to pass through the funnel to form a pile on paper at lower end of the funnel. The height (h) of the pile and distance across of the cone was noted. From the diameter, radius (r) was calculated. The angle of repose (Θ) can calculated by following condition.

$$\Theta = \tan^{1} (h/r)$$

Where, h = height of pile r = radius of base of the pile

ii. Bulk density: Bulk volume occupied by the mixed blend is noted using measuring cylinder. Bulk density is determined utilizing following formula

Bulk density (BD) = Mass of the mix / Bulk volume of the mix

iii. Tapped density: Tapped density is calculated by weighed amount of powder mix is filled the graduated cylinder, which is then tapped for 500 taps. Tapped density is determined by utilizing following formula

Tapped density (TD) = Mass of mix/ Tapped volume of the mix

iv. Compressibility index: Compressibility index indicate the tendency of formulation for binding. It shows the stream properties of the mix. Compressibility index was determined from the readings of bulk and tapped densities.

Compressibility index= (TD-BD) ×100/TD

Where, TD = Tapped density BD = Bulk density

v. Hausner's ratio: Hausner's ratio specifies the stream properties of the powder mix and is estimated by the proportion of tapped density to bulk density.

Hausner's ratio = Tapped density/Bulk density

vi. FTIR studies: IR spectra for pure drug and mini tablets formulations were verified in a Fourier transform infrared (FTIR) spectrophotometer.

vii. DSC studies: Differential Scanning Calorimetry (DSC) studies were accomplished for pure drug and optimal mini-tablets formulations. Perforated and sealed aluminum pans were utilized in the analysis for all the samples. Temperature calibrations were implemented utilizing indium as standard. An empty pan sealed in the similar manner as for the sample was utilized as a reference. The whole samples were run at a scanning rate of 10^0C/min from 50-300^{0}C.

6.2 Post compression Evaluations[16]:

viii. Weight variation: Weight variation test is led by utilizing advanced weighing balance. Twenty mini tablets were randomly chosen and weighed individually and calculated average weight. The percentage of weight variation was determined utilizing following formula:
% Weight variation = (Individual weight – Final weight)/Final weight X 100

Table 1: Weight variation standard limits

S.No.	*Average weight of tablet (Mg)*	*% deviation*
1	80 mg (or) less than 80 mg	± 10
2	More than 80 mg (or) less than 250 mg	± 7.5
3	250 mg (or) more than 250 mg	± 5

ix. Hardness: Mini tablets hardness of all the formulations was estimated by utilizing a Monsanto hardness tester. It is expressed in kg/cm^2.Hardness characterized as the force required to the break a tablet. Six mini tablets were randomly chosen from every formulation and the mean and standard deviations are determined.

x. Thickness: The thickness of ten arbitrarily chosen mini tablets from every formulation was individually noted in mm utilizing screw gauge and digital caliper.The mean and standard deviation values were determined.

xi. Friability: Twenty mini tablets are chosen randomly from every formulation and their initial weight (W_0) was distinguished and deposit in a friabilator. The friabilitor apparatus was rotated at 25 rpm for 4 minutes after mini tablets were detached. Mini tablets are weighed again (W_f).The percentage of friability was deliberated by utilizing following formula.
$\% F = (W_0 - W_f) / W_0 X\ 100$
Whereas, % F = Percentage of friabilityW_0 = Initial Weight W_f= Final weight

xii. Disintegration: The disintegration time of mini tablets was determined by utilizing disintegration test apparatus as per the provisions of Indian Pharmacopeias. One mini tablet was positioned in each of the six tubes of the basket. The apparatus was run utilizing 900 ml of dissolution medium as the immersion liquid. The assembly was raised and lowered between 30 cycles per minute in dissolution medium maintained at 37 ^{0} C. Then note down the disintegration time for mini tablets.

xiii. Drug Content: Drug content was determined by exactly weighing five mini tablets and crushing them in mortar. Then weighed extent of powder 5 mg of drug was transmitted to a 100 ml volumetric flask containing 100 ml of solvent. The flasks were shaken for solubilize the drug.1 ml of above solution was taken and diluted up to 10 ml and analyzed using UV visible spectrophotometer at lamda max. Estimate the drug content using concentration values obtained using UV.

xiv. In Vitro Dissolution Studies: In vitro dissolution studies were done by utilizing USP dissolution type 1 (basket) apparatus for Mini tablets enclosing in capsules and type 2 (paddle) apparatus for Mini tablets compacted as big tablet. In order to simulate the pH changes along with gastro intestinal tract three different dissolution media with pH 1.2 (stomach), 6.8(intestine) and 7.4(colon) buffers were utilized. The dissolution media were keep up at a 37 ± 0.5 ^{0}C temperature throughout the analysis and turn speed of basket kept up at 50 rpm(basket) or 100rpm (paddle).900 ml of dissolution medium was utilized at every time. When performing experiments for controlled release or delayed release dosage forms, the 0.1 N HCL was utilized for initial two hours meanwhile the average gastric emptying time is two hours, then dissolution medium was expelled and include new dissolution medium at pH 6.8 phosphate buffer for three hours, then evacuated the pH 6.8 buffer and include new dissolution medium at pH 7.4 phosphate buffer for residual rest of time (24 hours).A 5 ml of dissolution media was withdrawn at programmed time intervals and new dissolution media was exchanged. The withdrawn samples were analyzed by utilizing UV visible spectrophotometer and determine the cumulative quantity of drug release over the sampling times.

7. Conclusion

From this review it can be concluded that Pharmaceutical mini tablets offer numerous advantages over single unit dosage forms. Precise dose of drug can be assumed to patients to expand the efficiency. Mini tablets are alternative to pellets and granules when compared to single unit dosage forms. Though, production considerations must be carefully evaluated to ensure a good flow, complete and accurate filling of the die and destruction to the apparatus. Local irritation and dose dumping can be avoided by utilize of mini tablets. For those medications whose absorption is more in small intestine mini tablet dosage form is helpful as they can without much of a stretch go through the duodenum free of gastric emptying and intestinal motility. Bio adhesive mini tablets express improved bio adhesion and improved effect than that of single unit bio adhesive tablets. They are fit for pediatric and geriatric patient groups compare to single unit dose forms and also good substitutes for pellets and granules.

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