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Minitablets: Recent Trends and Developments with an update on Research and Patents

Sagar, Rajesh Kumar, Mangesh Pradeep Kulkarni, P.B. Vandana, Sheetu Wadhwa, Gurvinder Singh and Arun Sharma*

School of Pharmaceutical Sciences,
Lovely Professional University, Phagwara, Punjab, India – 144402.

(Corresponding author: Arun Sharma)*
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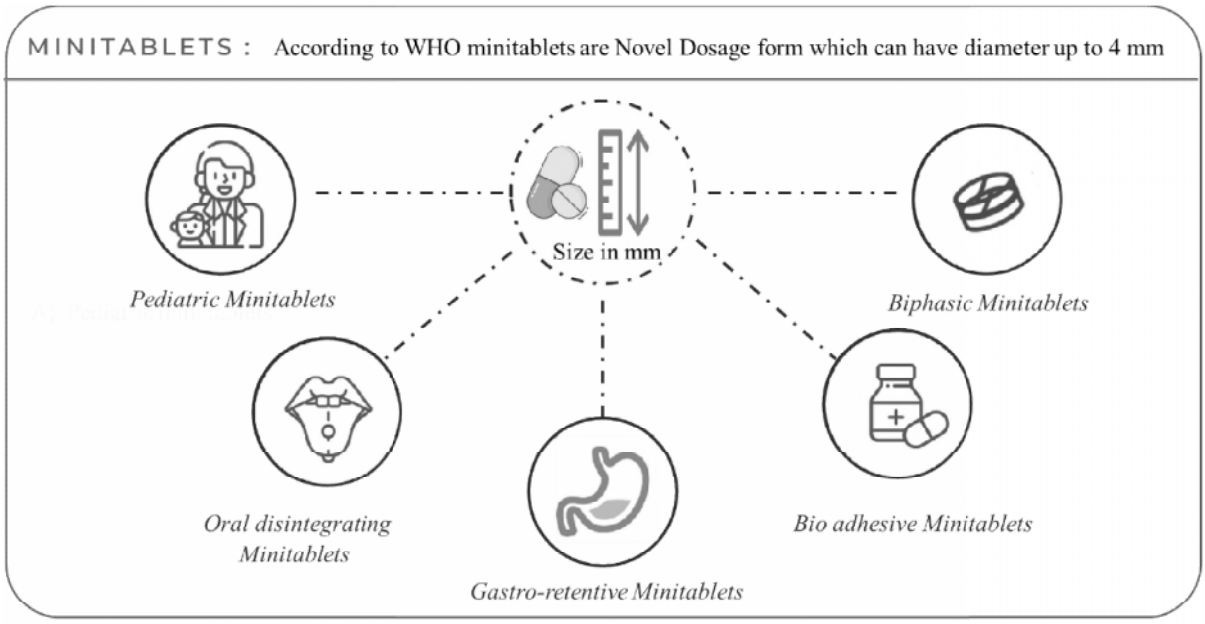
ABSTRACT: History speaks that oral dosage forms have been the most preferred ones amongst all the age groups of people because of their cost-effectiveness and minimal efforts of administration. However, conventional compressed tablets and capsules are associated with certain limitations associated to their varying plasma drug concentration, requirement of multiple dosing and difficulty in swallowing. Pharmaceutical Mini-tablets (MTs), seem to circumvent the above-mentioned limitation and can facilitate oral administration in pediatric and geriatric patients with minimal swallowing difficulty which can be attributed to their small diameter ≤4 mm. By reducing the fluctuations in drug release profile, MTs scan deliver the therapeutic agent efficiently with desired release pattern. The current paper is aimed to highlight the comparison of MTs with pellets, formulation and manufacturing techniques for MTs, their evaluation parameters, commercially available products, patents data on MTs, and a compilation of research work that has been done on mini-tables as a delivery system till date.

Keywords: Mini-tablets, oral dosage form, pediatrics, solid dosage form, floating dosage forms

Graphical Abstract



INTRODUCTION

Mini tablets (MTs) are one of the novel dosage forms that can be as small as 1mm in diameter (Tissen *et al.*, 2011). They can be defined as the novel dosage forms which can have diameter ≤3mm (Aleksovski *et al.*, 2015). MTs are generally compressed by the conventional compression technique but taking the size consideration in to the mind i.e., from 1-4mm. They possess the advantage of both solid and liquid formulations. Till now the pediatrics are given liquid formulation for administration because they possess advantage of ease in administration as well as dose of liquid formulation can easily be changed as per the requirement. Beside these advantages, they possess several disadvantages like low stability related to chemical and physical and microbial stability, limitation related to use of suitable excipient and types of preservative used for the preparation of pediatrics oral formulations. That's why MTs formulations seems

to be better alternative for pediatrics and geriatric population. If we see the previous studies and trends, we can find that the doctors and pharmacists do not prefer to prescribe tablets to infants and children below 6 years as it is very tough for them to swallow the whole tablet in intact form (Banker, 1970). But if we consider a study which was carried out back in 2009 on 100 children of age group between 2-6 years claiming a prominent result that MTs upto 3mm could easily be swallowed by the children without any difficulties (Aleksovski *et al.,* 2015). A recent study, 2mm diameter MTs were shown to be for immediate swallowing or chewing. The swallowing of MTs was found to be better than or similar to the administration of a syrup when given to children having age 0.5-6 years (Reddy & Ghosh, 2002). Study performed by Klingmann *et al.* (2014), clearly state that uncoated or coated 2mm MTs are well accepted by the children of age group 0.5-6 years. Study performed by the same author also determined that the uncoated MTs having diameter of 2mm dissolved rapidly and were accepted by neonates (Sastry *et al.,* 2000). The MTs was placed just near to the cheeks and swallowing was done with liquid or drink by parents' choice i.e., sugar solution, milk, breast milk or water. Result shows that the tablet was better accepted than 0.5ml of an oral syrup or suspension (Biradar *et al.,* 2006). Another study performed by panel of scientists concluded that children above 2 years swallow several mini tablets in a single dose if we use suitable glidants and suitable excipient (Lennartz & Mielck, 1998).

A. Advantages of mini tablets

- They possess less risk of dose dumping (Mastoi *et al.,* 2017)
- They can easily be customized as per the patient requirements.
- They possess high drug loading, wide range of drug release pattern (Tehseen *et al.,* 2013)
- They are easily reproducible and can be manufactured in continuous batch process.
- Manufacturing of mini-tablets is easy if we compared it with pellets.
- They offer excellent size uniformity, smooth surface and regular shape, weight, and equal dimensions (Keerthi *et al.,* 2014).
- They provide very less inter and intra subject variability in patient as they are too small in size.
- They have smooth surface, coating of MTs is easy with polymeric membrane or polymers which facilitate modified release.
- They show less local irritation in gastrointestinal tract (GIT) as the content spread throughout the GIT.
- They do not require any solvent for production (unlike pellets) which results in lesser stability.

Table 1: Comparison of mini-tablets and pellets based upon some specific parameters.

PARAMETERS	MINI TABLETS	PELLETS
Definition	Conventional tablets form having diameter 1-4 mm	They are small bead like structure that are filled in capsules or compressed in form of tablets
Solvent	Does not required any solvent for the preparation which overcome its stability problem	They required solvent for its production
Process	Can be prepared by conventional compression machine	Use of fluidized bed dryer spheronization extrusion required which make them a costlier preparation.
Physical characterization	They possess define size shape and uniformity	Usually, they are spherical in nature but are inferior in size shape and uniformity if we compared them with mini tablets
Coating	Can be coated into perforated pan coater an evenly coated due to their uniform surface	Coating of pellets is done by using Wuster coating technology which require more precision and skilled personnel
Packaging	Easily be packed into capsule sachets or stick packs	Generally dispensed into capsule

Mini tablets vs pellets. MTs are similar to pellets in terms of their size which sometimes causes a confusion between them. Though, the size range for pellets and MTs is somewhat similar, there are significant differences between them. Pellets can be defined as a multiparticulate drug delivery system having a size range between 0.5 to 2mm. Pellets possess several advantages like they improve the mechanical, chemical, physical properties (along with flow characteristics) of the powder. Table 1 shows the comparison between MTs and pellet and give a clear idea that how MTs are superior, and different from the pellet's preparation.

Multi-unit dosage system. For minimizing the dosing frequency, reducing potential toxicity and increasing treatment efficiency multi- unit dosage system was introduced because conventional (single unit) system failed to achieve this due to inconsistent plasma drug level leading to ineffectiveness of drug (Keerthi *et al.,* 2014). This leads to introduction of MTs dosage forms which improve the therapeutic efficiency and reduce the potential side effects. Multi- unit dosage system also has greater bioavailability compared to a single unit dosage form along with high dissolution profile (Lopes *et al.,* 2006).

Table 2: Comparison between single and multi-unit dosage.

Single Unit Dosage Form	Multi-Unit Dosage Form
High variability related to gastric emptying	Predictable gastric emptying
Nutritional status directly related to gastric emptying	Gastric emptying is not directly related to nutritional status
Inter and intra subject variability can be seen in absorption rate	Less Inter and Intra subject variability related to absorption rate
Chances of overdose and local irritation are very high	Less risk of overdose and local irritation

From the Table 2 we can get the insight towards comparison for single-unit dosage form and multi-unit dosage form.

B. Methods of Manufacturing Mini-Tablets

Enlisted methods can be used in the manufacturing of mini tablets

a. Direct compression
b. Wet granulation
c. Dry granulation
d. Melt extrusion.

a. Direct compression- Direct compression can be defined as a process in which tablets are compressed directly from blend (powder) containing active pharmaceutical ingredient (API) along with compatible or suitable excipients. In direct compression, the ingredients used are of compression grade (directly compressible) so as to attain the required hardness in the tablet (Jivraj *et al.,* 2000). Stability related issues are very less in directly compressed tablets in comparison to the tablets prepared by wet granulation technique (Jivraj *et al.,* 2000; Rao, *et al.,* 2011).

b. Wet granulation- It is the most widely used granulation process in pharmaceutical industries. In this technique, a binder solution is used to form a wet dough mass (Rieger *et al.,* 1986). The added liquid binds the moist powder particles by a combined action of capillary and viscous forces in the wet state. It is further passed through the sieve to form granules followed by drying. More permanent bonds are formed during drying leading to the formation of agglomerates. The granules are then finally compressed into the tablet by using conventional compression machine (Agrawal & Naveen, 2011).

c. Dry granulation- It is the first-choice technique used for the manufacturing of MTs of drug that are moisture sensitive and thermo labile in nature. Instruments like chilsonator or roller compactor is used along with compression machine. Premixed powder is passed through the rollers which are counter rotating with each other to form a thin ribbon or sheet. This sheet is brittle in nature and is reduced to a definite and proper size to form granules which are finally compressed in to tablet via using compression machine (Agrawal & Naveen, 2011; Lopes *et al.,* 2006).

d. Melt-Extrusion- In this technique, powder containing drug and excipients is premixed and then transferred to the melt extruder. Parameters like feed rate, temperature and screw speed are set in the range of melting point of the material. After the process, the resulted extrudate are collected milled and sieved respectively that results in formation of granules which are compressed into the final product i.e., MTs (Karthikeyan & Vijayalaxmi, 2013; Shah *et al.,* 2013).

C. Pre-Formulation Studies

Pre-formulation studies give the details about the nature of drug substance along with detailed frame work for pharmaceutical excipients, that results in final formulation. Following enlisted studies are performed as pre-formulation parameters for MTs.

Tapped and bulk density- Appropriate amount of powder is weighed and transferred into the measuring cylinder having a capacity of 100ml. Initial volume is noted for the further calculation. The density is calculated by-

$$\text{Density} = \frac{\text{Mass}}{\text{Volume}} \quad \ldots(1)$$

For tapped density USP tapped density apparatus (Taps-10, 500, 1250) can be used or the measuring cylinder can tapped by manually from a height of 2 cm at 1-2 sec of intervals until a constant volume reading is observed the final reading is noted and used for the further calculations (Chen *et al.,* 2010).

$$\text{Tapped Density} = \frac{\text{Mass}}{\text{Tapped Volume}} \quad \ldots(2)$$

Hausner ratio- Hausner ratio is generally calculated to know about the flow properties of the powder. Formula used for calculation

$$\text{Hausner Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}} \quad \ldots(3)$$

HR - <1.25 good flow of powder
HR- >1.25 poor flow of powder

Compressibility Index (CI)- CI is defined as the tendency of any selected powder to be compressed further when it is subjected to some external stress or pressure. Generally calculated by using the formula

$$CI = 100\,\frac{(Vo - VF)}{Vo} \quad \ldots(4)$$

V_O – Unsettled apparent volume
V_F – Final settled volume

Angle of repose- This experiment is done by using a fixed funnel from which a calculated amount of powder is passed through the funnel. Funnel is kept at a height denoted by (h) 2cm above the paper that is placed on a flat surface. Using the given formula angle of repose is calculated

$$\Theta = \tan^{-1}\frac{h}{r} \quad \ldots(5)$$

Were, h= height of heap and r = radius of heap

D. Types of Mini Tablets

MTs can be classified based upon the target site, patient need and method of manufacturing-

a. Pediatric MTs.
b. Oral disintegrating MTs.
c. Gastro-retentive MTs.
d. Bio adhesive MTs.

e. Biphasic MTs.

a. Pediatric Mini-Tablets: For children, the most common dosage forms are capsules, syrup, and tablets. Syrups are liquid dosage forms having large amount of sugar content and are simple in administration with additional advantage of dose alteration as per the requirement of the patient. Besides all these advantages, syrups possess limitations associated with them such as they are liquid preparations, and thus, they are physically, microbiologically, and chemically unstable, have issues in taste masking and there is less scope to offer controlled drug release. In contrast to MTs, tablets are bigger in size which make them inconvenient for pediatric patient to swallow as a one dose. Moreover, the dose adjustment is not an easy task and as a general practice, tablet is divided into two halves which is not a correct approach. MTs, provide us a suitable platform to overcome the aforementioned limitations and it is further accepted by children with no trouble (Singh *et al.,* 2018). Lavan *et al.,* (2021) formulated pediatric MTs, having a diameter of 2 mm that was synthesized by employing lapatinib amorphous solid dispersion (ASD) comprising hydroxypropyl methylcellulose phthalate (HPMCP) and hydroxypropyl methylcellulose E3(HPMCE3). Formulated MTs were further evaluated on the basis of weight, dimension, tensile strength, percent friability. Formulated MTs were subjected to animal study where *Tmax* and area under curve (AUC) was evaluated (Lavan *et al.,* 2021).

b. Oral disintegrating mini tablets (ODMTs)- These are the novel dosage forms which get rapidly disintegrated in the mouth within 1 to 3 min without chewing it and there is no requirement of water unlike we use it for conventional dosage forms. ODMTs have other synonyms too like “rapid disintegrating tablets”, “mouth dissolving”, “crunch melt tablets”, “orodispersible tablets”, “bite dispersible tablets”, “quick dissolve tablets” (Hahm & Augsburger, 2008). These tablets are more convenient for pediatrics because they are small in size as well as they rapidly dissolve in mouth. Stoltenberg *et al.,* (2011) formulated novel ODMTs based on mannitol using direct compression method by employing conventional tableting machines. Developed ODMTs were of 2 mm in diameter that owned promising role as oral solid dosage form for pediatric usage (Stoltenberg & Breitkreutz, 2011).

Every ODMT’s must have enlisted properties so as they can widely accepted

- Disintegration of these tablets should be fast.
- Should disintegrate in mouth without using additional liquid like water or sugar solution.
- After disintegration they must be converted into soft paste.
- If drug is having undesirable taste masker must be use.
- It does not affect the normal functioning of taste buds present on the tongue (Singh *et al.,* 2018)

c. Gastro-retentive Mini Tablets- These MTs are generally used to target the GIT they are intended to release drug in stomach for prolong period of time. Generally, these MTs float on the surface of GI fluid as they are formulated by using gas liberating or gas generating agents. When they come in direct contact with the GI fluid, they liberate CO_2 which get entrapped inside the swellable polymer that decrease the density of the formulation and tablets float on the surface of GI fluid. In normal size, gastro-retentive tablets drug loading is low as the amount of swellable polymer is high, but MTs can be easily coated by sodium bicarbonate, sodium carbonate or eudragit, leading to high drug loading. Fluid bed processor (FBP) can be used to coat the MTs. Goole *et al.,* (2008) prepared sustained release MTs of levodopa which had diameter of 3-mm along with gas generating agent and core is coated with eudragit RL30 D to ensure the desire release of drug from the MTs (Thomson *et al.,* 2009).

d. Bio-adhesive mini tablets-Bio-adhesive polymers can be defined as the polymers, which when comein contact with moisture they stick together with surface as they have high viscosity even at low concentration (Biradar *et al.,* 2006). Bio-adhesive MTs are generally used to deliver the drug in vaginal area for prolonged period of time. These tablets work on the principle of swelling and forming micro gel, that results in controlled drug delivery of desired drug through which anticipated therapeutic action can be achieved. Several marketed dosage forms are easily available for vaginal infections like creams, gels, ointments and, tablets etc. Major problem associated with these dosage forms are leakage, messiness, less retention time, and patient non-compliance. Nano formulations can be used as an alternative to conventional formulations but major disadvantage with those preparation is low residence time as they are in liquid form. So, to resolve all these problems, the MTs coated with bio adhesive polymers can be suitable approach (Hiorth *et al.,* 2014). Hiroth *et al*, prepared bio-adhesive mini tablet of hexyl ammonium hydro chlorodium (HAL) which is majorly used in treatment of cervical cancer by photodynamic therapy. Thermo gel of HAL is also present but HAL is unstable in moist environment, so to eliminate its stability related issue, bio-adhesive mini tablets were introduced which were prepared by direct compression technique (Katakam *et al.,* 2014). Hydroxypropyl Methylcellulose (HPMC) and Hydroxypropyl Cellulose (HPC) were used as adhesive polymers which showed adequate mechanical and bio-adhesive strength. For maintaining the pH, they used non-ionic cellulose ether with adhesive property as the pH of vagina differs from individual to individual (Katakam *et al.,* 2014).

e. Biphasic mini tablets- these system are designed I such as way that they comprise of two sections i.e., fast-releasing and slow-releasing part (Bhesaniya & Yadav, 2018). When the biphasic MTs are administered, fast releasing portion releases drug immediately after the administration, while the second part releases drug at slow and steady rate in controlled manner. This kind of preparations is most suitable for hypertension patients owing to reduced frequency of dosing. Various drugs can be compressed in the form of

mini tablets and can be filled in capsule to treat more than one disease at a time. Lopes *et al*. (2006) prepared biphasic mini-tablet having ibuprofen as a drug with ideal release characteristics.

E. Mini-Tablets as a Modified Drug Delivery System

Several techniques were employed to modify the release of the active pharmaceutical ingredient from the dosage form like targeted drug release, pulsatile and Pulsatile release (Aleksovski *et al.,* 2015). These techniques of release modifications have been explained briefly further.

- **Extended release-** In this type of system, the active substance is released gradually for an extended period of time (Kumar *et al.,* 2012). This type of release can be achieved by two means; a) by extending the transition time over GIT; b) by modifying the diffusion rate of drug directly from the dosage form. Extended release of drug can be achieved by changing the diffusion and dissolution of drug by employing a barrier coating or by converting it into matrix system (Obaidat *et al.,* 2015).
- **Targeted drug release:** These are also called as smart drug delivery systems as they are capable of delivering the loaded drug to the desired or specific target inside the living organism or to human body parts. Targeted drug delivery systems enable the drug to exhibit localized effect and assist further to attain prolonged therapeutic effect. These systems further diminish the frequency of the dose administration in the patient, hence, reduce the side effects associated with it which can be attributed to the avoidance of fluctuation in the drug concentration in the blood. Hadi *et.al.* (2014) formulated novel pH responsive targeted MTs of 3 mm in diameter comprising of naproxen that aimed towards the chronotherapeutic treatment of rheumatoid arthritis. Formulated MTs were further examined for possible interaction by employing FTIR and DSC, where data suggested no interaction between selected excipients and drug. Developed MTs were found to be stable for 6 months and more interestingly, 99.4% of drug was released within 8 hours as revealed through drug release studies (Hadi *et al.,* 2014).
- **Pulsatile release-** Physiological factors like heart rate, blood pressure, enzymes concentration, plasma proteins and hormones greatly affect the drug bioavailability. To resolve these problems, distinct drug delivery modes have been opted so far, one such delivery system is pulsatile release system. It is also known as a time-controlled system as it responds according to the circadian rhythms of the patient (Bayan *et al.,* (2021) (Firoz *et al.,* 2020). This system is most beneficial in conditions such as asthma, angina pectoris etc. Pulsatile release can be obtained by coating the tablet with a controlled release polymer which also acts as a protective layer for the drug (Roy & Shahiwala, 2009). Chaudhary *et al.,* (2015) had formulated pulsatile release MTs of urapidil filled in the gelatin capsule. Mean diameter of 6 mm was reported and the formulated MTs were coated using eudragit S-100 which offers pulsatile release of the selected drug.

  Table 3 comprises the list of commercially available Mini-tablets and Mini-tablets in capsule dosage form.

Table 3: Example of commercially available mini tablets.

Dosage form	Brand Name	Drug name	Indication	Manufacturer
Mini-Tablet	Aricept	Donepezail hydrochloride	Alzheimer's/Dementia	Eisai
Mini-Tablet	Alesse	Levonorergosterol and ethinyl estradiol	Contraceptive	Wyeth-Ayerst
Mini-Tablet	Accolate	Zafirlukast	Asthma	AstraZeneca
Mini-Tablet	Coumadin	Warfarin sodium	Anticoagulant	Bristol-Myers Squibb
Mini-Tablet	Exalgo	Hydromorphone Hcl	Moderate to severe pain	Mallinckrodt Inc
Mini-Tablet	Effient	Prasugrel tablets	Prevent blood clotting	Activz Lifesciences India Pvt Ltd
Mini-Tablet	Razadyne ER	Galantamine HBr	Alzeimers	Johnson & Johnson
Mini-Tablet	Treximet	Sumatriptan and Naproxen Sod.	Migraine	GSK
Mini-Tablet	Trilipix	Fenofibric Acid	Reduce abnormal blood lipid level	AbbVie| FiercePharma
Mini-Tablet	Zyprexa	Olanzapine	Schizophrenia	Eli Lilly & Co.
Capsule	Lamisil	Terbinafine Hcl	Antifungal	Novartis
Capsule	Orfiril long	Sodium valproate	Epilepsy	Desitin
Capsule	Pankeratan	Pancreatin	Pancreatic insufficiency	Novartis
Capsule	Enzyme-Lefax	Pancreatin	Indigestion	Bayer
Capsule	Rythmol SR	Propafenone HCl	Antiarrhythmic	GSK
Capsule	Ultresa	Pancrelipase	Pancreatic insufficiency	APTALIS Pharma US
Capsule	Zontivity	Vorpaxar tablet	Antiplatelet agent	Sun Pharmaceutical
Stick pack	Kalydeco	Ivacaftor	Cystic fibrosis	Vertex

F. Method of Administration

MTs can be administered to a patient via suitable methods that are listed below and their key parameters are demonstrated in Fig. 1:

Direct administered in single dose- MTs preparation is administered as a single unit dosage form through oral rout. Prescribed dose can easily be taken and these tablets are packed in suitable pharmaceutical grade container. Few report suggests that the mini tablets are again compressed to get a normal size tablet (Thomson *et al.,* 2009).

Filled in gelatin(hard) capsules- Handling of MTs can be difficult for the patient as the size of the tablet is very small so there is a possibility of getting inaccurate dose of the drug. To overcome this kind of possibility, the tablets are filled in capsules and then administered to patient (Bechgaard *et al.,* 1978).

Automatic dosing devices- Inaccurate administration of dose result in adverse effect or decrease efficiency of specific drug. Sometimes patient might administer half tablet which may result in proper pharmacological effect. In such cases an automatic dose dispensing device can be used to dispense require dose of mini-tablets (Rosenson, 2006).

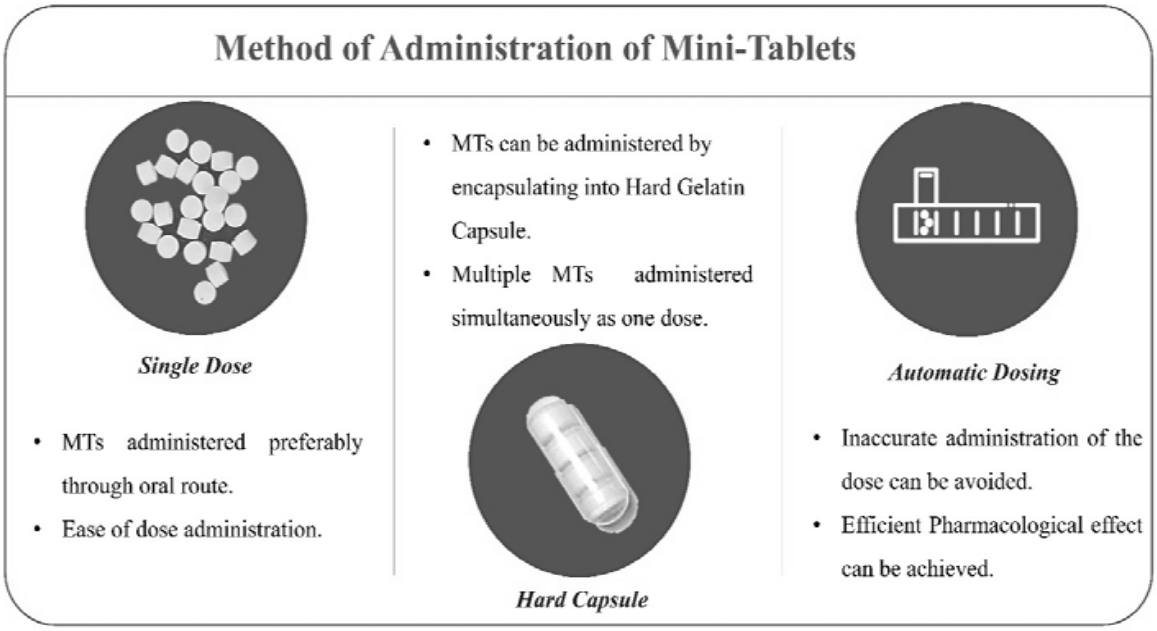


Fig. 1. Different modes of administration of minitablets.

G. Evaluation Parameters of Mini Tablets

Thickness- Uniformity in the thickness of the MTs is of great importance hence, it should be maintained all throughout the same a lot and even should comply with batch to batch. Thickness of the MTs is being calculated by using either normal vernier caliper or by digital vernier caliper and it can be up to 2.5 mm (Peacock, 2014). Screw gauge is also applied to calculate the thickness of MTs which is further denoted in 'mm' (Zhu *et al.,* 2005).

Friability- For MTs with an average weight of 0.65 g or less, a sample of whole tablet correspond to 6.5 g should be taken and for the MTs with an average weight more than 0.65 g, sample of 10MTs is taken and then transferred to the Roche friabilator. Drum rotate at a speed of 25 rpm for 4 min afterward the MTs were taken out from the drum, dedusted and weigh. Friability is given in terms of percentage i.e., it should lie in the acceptance range which is less than 1% (Smoleńska *et al.,* 1999).

Hardness- Hardness is calculated by Monsanto hardness tester or Pfizer hardness tester in which the unit is expressed in kg/cm^2. It is calculated by using either electrical or automatic hardness tester in which the unit is expressed in N (Srinarong *et al.,* 2009).

Weight variation- Twenty MTs are randomly selected from the batch and then weighed individually. Average weight is calculated and as per the USP criteria, it should not be less than 90% or more than 110% of the average weight.

Drug content uniformity-Crush five MTs through radially available mortar pestle and measure the weight of resulting powder which contain equivalent to 10mg of drug. Afterwards, transfer the powder in 10 ml of dissolution medium to make a concentration of 100µg/ml. Take a 15ml of solution, dilute it further upto 100ml to make a final concentration of 15µg/ml and measure the absorbance by employing UV visible spectrophotometer at specific wave length.

***In- Vitro* drug release-** Simulated gastric and intestinal fluids are been used to determine the release pattern of the MTs(Vogt, Kunath, Dressman, & Biopharmaceutics, 2008). Study related to drug release is carried out in USP dissolution Apparatus-I, sustaining a temperature at $37\pm0.5^{\circ}C$, rotating speed at 100 rpm and pH 1.2 for 2 hours, as the average gastric emptying time is around 2 hours.

Dissolution buffer is changed to 6.8 pH and experiment is continued for another 10 hours (Priyanka *et al.*, 2018). At pre-determined time interval 5ml of the solution is withdrawn and replaced with drug free dissolution medium. The withdrawn sample are then analyzed by using UV- spectrophotometer.

H. Patent

Patent is a property right granted to an inventor for his/her novel contribution in the scientific community and it is approved by respective sovereign authority. Various scientists have worked in the field of mini-tablet and their work is comprised in the Table 4 in form of patents.

Table 4: List of patents representing distinct minitablets.

Sr. no.	Patent no.	Patent title	Approval Date	Reference
1.	USOO6110494A	Cisapride Mini-Tablet formulations	Aug. 29, 2000	(Clancy & Cumming, 2000)
2.	US006046177A	Sulfoalkyl Ether Cyclodextrin based Controlled Release Pharmaceutical Preparation	Apr. 4, 2000	(Stella, Rajewski, Rao, Mcginity, & Mosher, 2000)
3.	US 2005/0120829A1	Method for the production of High Concentration Manganese Mini-Tablet for allowing Aluminium bath device for Implanting SAD method	Jun. 9, 2005	(Guerrenabarrena, Hernandez, Bravo, Ganuza, & Fernandez, 2005)
4.	WO2007/106960A1	Controlled-release floating dosage forms	Sep. 27, 2007	(Vanderbist, Baudier, Deboeck, Amighi, & Goole, 2006)
5.	US2007/0224260A1	Dosage form having Polymorphic stability	Sep. 27, 2007	(Mehta, Bhushan, Chowdary, Krishnan, & Mohan, 2007)
6.	US2007/0224259A1	Anti-inflammatory pharmaceutical preparation	Sep. 27,2007	(Gupta, Kodipyaka, Gore, Bhushan, & Mohan, 2007)
7.	WO2010043950A2	Propafenone Extended-Release Composition	Apr. 22, 2010	(Anand, Sathurappan, Sankaranarayanan, & Chelamkuri, 2010)
8.	US8,093,261	Rapid Release Mini-tablet	Jan. 10, 2012	(Guarnieri, 2012)
9.	US2012/0141584A1	Multi-layer Mini-tablet	Jun. 7, 2012	(Chauhan & Nutalapati, 2012)
10.	US2013/0129824A1	Solid Drug Tablet for Implantable Drug Delivery Devices	May. 23, 2013	(Daniel, Hutchins III, Larrivee-Elkins, & Lee, 2013)
11.	US8,945,616B2	Controlled Release Budeosnide Mini-tablets	Feb. 3, 2015	(Murty & Li, 2015)
12.	US2015/0238425A1	Mini-Tablets	Aug. 27, 2015	(Meesters & Spros, 2015)
13.	EP3187176A1	Paliperidone mini tablets	Jul. 05, 2017	(Turkyilmaz, Zenginer, & Yag,, 2017)
14.	US2020/0054530	Dosing Device for Measuring and Dispensing Mini-Tablet	Feb. 20, 2020	(Berenshteyn, Gotliboym, & Granelli, 2020)
15.	US10,722,494B2	Melatonin Mini-Tablet and Method of Manufacturing	Jul. 28, 2020	(Laudon & Zisapel, 2020)
16.	US2020/0237672A1	Mini-Tablet	Jul. 30, 2020	(Van Den Heuvel, Van Laarhoven, Janssen, & Van Haandel, 2020)

CONCLUSION

If we compare MTs with conventional compressed tablets or single unit dosage forms, the MTs provide us several benefits which make them better alternative for pellets and granules. Moreover, MTs provide the benefits of combination therapy that is difficult to acquire through conventional solid dosage form. MTs have high mechanical strength and low porosity, it can be easily compressed into large size tablets or can be filled inside the capsule. Additionally, MTs increase the patient compliance, enhance the localized effect of the selected drug and avoid the dose dumping. MTs are most beneficial to the drug that are absorbed from small intestine, because they can easily pass-through the duodenum independent of gastric emptying and intestinal motility. As discussed in this review, MTs can be employed as a promising drug delivery system for pediatric as well as for geriatric patients. Recent novel work complied in the present paper will further provide a vivacious information platform to the young researchers to come up with novel ideas to solve the problems associated with the conventional drug delivery systems.

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