International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1766-1773 www.ijprajournal.com ISSN: 2249-7781

# Drug Delivery System for Pediatric Dosage Form: A Review of Minitablet Technology and Its Manufacturing Perspectives

Dr. Ashish P. Gorle[1]*, Sunil Dongre[1]*, Manoj Deore[2], Asmita Gunjal[2]
R.C. Patel Institute of Pharmacaeutical Education and Research, Shirpur-425405, Maharashtra, India

Submitted: 15-04-2024 Accepted: 25-04-2024

**ABSTRACT**
Mini tablets, recent trend of solid dosage form, made remarkable contribution to avoid certain obstacles in people's mind and offered best therapeutic benefits, flexible dose and combined released pattern. Mini tablets were developed and reported as patient friendly with increased patient acceptance. Mini tablets were made into modified release system for better dose and prolong drug release. They offer the advantage of reduced dose dumping and increased effect of drug by localization. Manufacture of mini tablets are similar to conventional tablets but need a change in tooling, equipment and specifications. Evaluation parameters found to be similar with conventional tablets but doses are variable. Mini tablets can also be encapsulated and hence different drug combinations are tried and found useful.

**Keywords:** Mini tablets, Oral dosage forms, Manufacturing, Dose, Multi tooling punches, Capsule

## INTRODUCTION

The development of pediatric formulations, particularly those suitable for very young children, can be challenging to the pharmaceutical industry and research [1]. There is only limited knowledge available on the acceptability of different dosage forms, administration volumes, dosage form size, taste, and the safety of formulation excipients in relation to the age and development status of the child [2]. Available solid formulations may be impractical due to the inability of paediatrics to swallow conventional tablets [8,9]. Moreover, some physicians may require an increase in the dose by 0.1 mg, which cannot be achieved by using the available tablets; as tablet breaking will not guarantee accurate dosing, or by using liquid formulations; due to inaccurate volume measuring. The production of a palatable dosage form is very important for patient compliance, especially for pediatric population [10]. Thus, bitter taste masking is an important consideration in the formulation of many therapeutics which may suffer from unacceptable taste, the principle of taste masking depends mainly on minimizing the direct contact between the bitter drug and the taste receptors in the buccal cavity of the subject [11,12]. The palatability of pharmaceutical product could be achieved through many techniques, which do not only improve the taste, but also the stability of the drug in the formulation and acceptability of the final product [13,14]. Minitablets can be defined as small tablets with a diameter of 5 mm or less [15] or even the size could be more restricted to be less than 3 mm [16], they can be formulated easily through conventional tablet presses. The ability to swallow minitablets and its safety of use o has been recently reported for young children, in infants and toddlers (1 month to 2 years), depending on the tablet's properties [17]

Orally disintegrating minitablets (ODMT) have gained much interest in the past decade [20], combining advantages of ODT including palatability together with the safety and ease of modulation of minitablets, in addition to the small size which helps in the ease of dose control as well as avoiding chocking for paediatrics in case of ingestion [21].

Oral controlled release drug delivery systems can be classified in two categories:

- Single unit dosage forms: Tablets or capsules
- Multiple unit dosage forms: Granules, pellets or mini-tablets.
- Mini- tablets are novel multiple unit solid dosage form which are in the size equal to or smaller than 3.0 mm in diameter.

**I. Minitablet technology:**

- Mini- tablets are novel multiple unit solid dosage form which are in the size equal to or smaller than 3.0 mm in Diameter.
- Over a decade now fast disintegrating mini-tablets (FDMTs), have gained enormous popularity for better patient compliance and Acceptance.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1766-1773 www.ijprajournal.com ISSN: 2249-7781

- FDMTs ease of administration without water and provide the fast onset of action is also the reason for their gaining popularity in the general Population.
- Also, FDMTs have the proven potential in increasing the bioavailability of low aqueous soluble drug through fast disintegration and enhanced dissolution rate.
- Mini-tablets have many advantages over other dosage forms, such as ease of transportation, application and production, high patient compliance, accurate dosing, control of drug release and stability.
- However, the desired release profile, therapeutic effect or ease of use in pediatrics or geriatrics, difficulty in swallowing may not be achieved by conventional tablets.
- These factors, such as repetitive dosing, unpredictable absorption and undesirable toxicity lead to the development of controlled drug delivery system.
- Mini-tablets produced on conventional presses equipped with multiple tooling. This production is similar to the production of standard tablets but requires excellent powder flow due to the small dies, exact control of process parameters and special caution during tablet press assembly in order to avoid tool damage.
- Mini-tablets (coated or uncoated and single or multiple-unit systems) are mainly developed as patient-friendly systems for pediatric and geriatric patients and also for personalized medicine because they offer improved swallowing and flexible dosing, combining various release kinetics, doses and active compounds in only one system.
- Mini-tablets may also be successfully used as multiple-unit modified release systems (extended release, delayed-colon release, pulsatile and bi-modal release and gastro retentive systems) providing improved drug bioavailability compared with single-unit systems.
- Mini-tablets (coated or uncoated and single or multiple-unit systems) are mainly developed as patient-friendly systems for pediatric and geriatric patients and also for personalized medicine because they offer:

  Combining various release kinetics

  Flexible dosing

  Improved swallowing

  Doses and active compounds in only one system

| Sr No. | Advantages | Disadvantage |
|---|---|---|
| 1. | Decrease dose dumping | Price maybe higher depending on production technology |
| 2. | Decrease inter-intra patirnt variability | Requirement of excellent powder flow due to small dies |
| 3. | Good coating substrate | Repturing of coating ny accidentlyor chewing |
| 4. | Decrease local irritation | Limited drug loaing capaacity per tablet |
| 5. | Decrease capping tendency | Multiple dosing might be needed due to limited drug load per single unit |
| 6. | Fine tuning of release rate | Packing platforms needed to be developed |
| 7. | Allow co-existance of different or incompatible drugs | Dosing administration frequency and route needs to be distributed |

Table 01:
Advantage & disadvantage of minitablet

**Figure 01: Minitablet formulation**

## II. Methods of manufacturing mini tablets:

**Direct compression technique**: This is a process where the powder mixture holding API and

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1766-1773 www.ijprajournal.com ISSN: 2249-7781

excipients which can be compressed directly into biconvex mini tablets. Direct compression grades have been used to achieve the required hardness. Problems of stability were found lower than those of tablets with wet granulation.

**Dry granulation technique**: This technique is used to develop thermo-labile, moisture-sensitive tablets. A roller compactor or chilsonator processing equipment can be used for these techniques. This machine compresses under extreme pressure as premixed powders have been found in the shape of a brittle ribbon, board, or fragment between two counter spinning rollers. By employing 'slugging' techniques granules can be produced, where slug is screened or milled and granules are mixed and finally compressed with other excipients.

**Wet granulation**: This technique involves using binder solution to form granules which are further compressed into mini tablets.

**Melt-extrusion technique**: The premixed powder API and excipients is allowed to move towards melt-extruder. In the melt extruder material range, a speed of the screw, feed rate and temperature parameters can be set. Then the extrudates are milled and sieved. Using a compression tool, the granules collected are then compressed into mini tablets.

**Possibilities of Formulating Mini-Tablet Dosage Forms:**

- Compressed mini-tablets
- Encapsulated Coated mini-tablets
- Compressed mini-tablets presented as a biphasic drug delivery system

**Mini tablets can be classified based into:**

- Pediatric mini tablets
- Oral disintegrating mini tablets
- Gastro retentive min tablets Bio-adhesive mini tablet
- Biphasic mini tablets
- pH responsive mini tablets
- Biphasic mini tablets

**III. Manufacturing of Mini-tablets:**

Despite the increasing importance of mini-tablets for its advantages as pediatric formulations and in modified-release applications, its popularity is limited due to the lack of formulation and processing knowledge in developing such dosage forms. The development of minitablets as a Drug Product (DP) is mainly dictated by the type of dosage form required, physico-chemical properties of the active ingredient, and other excipients and factors related to the manufacturing process. Depending on the nature of the active ingredient, the most common manufacturing process for mini-tablets includes blending operations, compression of the final blend into mini-tablet cores, coating minitablet cores and finally packaging of the coated mini-tablets into appropriate packaging configuration

**IV. Physical properties of blend:**

The current drug development pipeline has many molecules with poorly aqueous solubility. These drug candidates are typically developed into their different salt forms or processed as Amorphous Solid Dispersion (ASD). Some challenges observed during pre-formulation with such salt and crystalline forms include poor flow properties, electrostatic effects and low densities due to very fine particle size. When a high drug load is required, challenges related to flow is magnified. When a drug molecule is electro static in nature, sticking to the wall of the blender which can lead to low assay and blend uniformity issue is observed. In some cases, additional granulation (dry or wet) is required to improve flow properties by controlling particle size of the generated granules. It is important to avoid very large granules that could also cause inadequate flow by blocking the space within the die during compression. The ideal flow should be such that it supports consistent die filing. Sticking is another problem due to drug molecule.

This can be avoided by adequate lubrication during a pre-mixing step. Early development work related to excipient screening based on particles size and selection of processing parameters for granulation determines the quality of the final blend which ultimately controls blend uniformity. So, proper characterization and optimization of powder blends should include densities (bulk density/BD and tapped density/TD), flow properties, and segregation potential. The selection of different grades of excipients is also important to evaluate critical material properties required for successful development of mini-tablets with specifically small size (≤ 2.0 mm).

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1766-1773 www.ijprajournal.com ISSN: 2249-7781

**V. Compression of mini-tablets:**

The main difference in tableting between regular size tablets and mini-tablets is type of tooling required. Generally, tablet press to manufacture mini-tablets are using standard reciprocating or a rotary tablet press with single or multi-tip tooling [11,17].

However, certain modifications to the press or/and tooling might be necessary [18,19] depending on tableting requirements. Compression with a single-tip die or tooling with a low number of tips is not practical commercially due to slow output of mini-tablets and thus a long run time.

The multitip tooling must meet certain requirements regarding precision and mechanical stability. It is typically more expensive compared to the standard tooling of normal size tablets. Depending on the type of the press, tooling, and size of the mini-tablets, up to 26 tips or even more tips can be accommodated on a punch.

**Figure 02: Multi-tip punch technology**

Multiple-tip tooling has a key similar to the tooling designed for non-round tablets for orientation. Mini-tablets compressed with deeply concaved tooling can have larger tablet density gradients compared to standard or shallow concave designs. Such gradients can lead to tablet attrition during coating, packaging, or other handling steps. The use of tapered die designs can decrease residual stresses, resulting in smaller and fewer micro defects resulting in more robust mini-tablets. Recessed dies are also advisable to protect the punch tips. Effective control over the feed frame is critical as tablet ejection can be challenging. This requires an optimized setup with precise adjustment of specially designed scraper blades to limiting tablet jumping. Multiple-tip punches are available as multiple-part assemblies or as monoblock from tool suppliers. Monoblock punches offer faster tooling installation and easier cleaning, can be manufactured to tighter tolerances, as well as are more resistant to tip breakage than assembled multiple part tooling. However, multiple-part punches allow the replacement of damaged punch parts [20]

| Brand Name | Drug Name | Indication | Manufacturer | Dosage Form |
|---|---|---|---|---|
| Rythmol® SR | Propafenone HCl | Antiarrhythmic | GlaxoSmithKline | Capsule |
| Enzym-Lefax® | Pancreatin | Indigestion | Bayer | Capsule |
| Lamisil® Oral Granules | Terbinafine HCl | Antifungal | Novartis | Sachet |
| Orfiril® long | Sodium Valproate | Epilepsy | Desitin | Capsule, Sachet |
| Pankreatan® | Pancreatin | Pancreatic Insufficiency | Novartis | Capsule |
| Trilipix® | Fenofibric acid | Cholesterol | Abbott | Capsule |
| Kalydeco® | Ivacaftor | Cystic Fibrosis (CF) | Vertex | Stick Pack |

**Table 02: Example of Commercially available mini-tab products**

A certain degree of care should be applied when handling and using mini-tablet tooling as it is easy to damage. Multi-tip tooling must meet tighter requirements for machining and mechanical stability compared to larger tablet tooling. This labour-intensive manufacturing leads to higher production costs. Any excessive force applied to the tooling can lead to damage of punches. Due to the small diameter of the punches, they are easy to deform and break. Therefore, careful handling and following the manufacturer recommendations for the maximum compression force is essential. If multiple tip tooling is used, then the maximum compression force value will be higher and is typically recommended by the tooling manufacturer.

The surface area/ weight ratio of mini-tablets is significantly higher than that of normal size tablets. This results in higher ejection forces during compression and may potentially result into

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1766-1773 www.ijprajournal.com ISSN: 2249-7781

"sticking" issues. Therefore, during development, higher levels of lubricant needs to add to offset any "sticking" issues. Shallow convex mini tablets have improved uniform density distribution throughout the core, which can lead to a more robust compression process. Deep convex mini-tablets roll more effectively, and are more suitable for tablet counting technologies commonly used by sachet filling and encapsulation machine providers. The weight uniformity of mini-tablets is crucial because it impacts content uniformity and dosing accuracy. In cases where the blend is containing relatively small particles, extra processing steps such as fluid bed granulation, high-shear granulation, or roller compaction may be required in the manufacturing process to improve flow properties. It is also important to control or minimize friability of mini-tablets by optimizing tablet press speed. It has been noticed that higher press speeds can contribute to higher friability or fragmented mini-tablets. Typically, the optimum ratio of particle-to die diameter to minimize weight variability in tablet compression is between 1:20 to 1:30. A large proportion of particles larger than the optimum ratio in mini-tablet manufacturing can lead to increased tablet weight variability. The tolerance for weight variability in mini-tablets is smaller than for larger tablets. Small absolute weight variations will lead to more significant relative variations in potency. The weight checks of mini-tablets need to be assessed using high precision analytical balances with high accuracy (≤ 0.001 mg). Additionally, hardness and thickness need to be measured as in-process controls during compression process. This may require a hardness/thickness tester which is capable of handling mini-tablets. The tablet press has to be equipped with force feeder as compared to gravity feeder to reduce weight variability. These challenges to monitor and control physico-mechanical attributes, sensitive characterization techniques and thus the specialized equipment needed for these measurements results in an increases manufacturing cost.

## VI. Packaging of Mini-Tablets:

The packaging configuration of mini-tablets is mainly dictated by the target product profile or product design requirements. The selection of correct packaging configuration also depends on drug product performance in a particular packaging configuration during long term storage. There are number of ways to deliver mini-tablets to the patients, these include encapsulation in capsule shells, packaged into unit-dose packaging such as stick-packs or sachets, or prefilling a container for disintegration.

## VII. Encapsulation of mini-tablets:

Among the possible packaging configurations, encapsulation of mini-tablets is preferred option. The encapsulation machines are capable to fill mini-tablets, pellets, powder, and granules with direct or indirect filling operation mechanism. In the case of direct filling operation, the mini-tablets are fed into the body until it is completely full. An encapsulator such as the Qualifill TM Pellet filler works on direct filling operation mechanism.

For indirect filling, operation the encapsulates have modified d osators that use either suction to hold the material in the tube during transfer or are pushed through the material bed as seen in Zanasi 40 E encapsulator. However, most advanced encapsulation equipment currently on the market is units such as Bosch GKF 2500. These machines offer filling of minitablets based on number of individual mini-tablets per capsule. Table 03 represents number of mini-tablets of 2 mm size can be filled in different capsule size. Custom designed dosing discs with cavities deliberate to be filled with mini-tablets are used.

Each dosing disc is designed to accommodate the specific size of the mini-tablets and count required per capsule. A variable thickness dosing disc can slide underneath to hold the material prior to transfer to allow only one mini-tablet per cavity. The mini-tablets are held in position on the wheel by vacuum, and this is electronically monitored by a webcam sensor which checks the disc for the presence of mini-tablets. All insufficiently filled capsules are automatically rejected in the finished product discharge chute. The dosing discs are intended to count mini-tablets in an accurate manner across a wide range of target fills. A pilot scale encapsulator such as the Zanasi 40 E is capable of filling capsules at relatively moderate speed of around 40,000 capsules per hour whereas the Bosch GKF 2500 can be used for commercial scale and is capable of filling capsules at speeds of 150,000 capsules or more per hour. Moreover, modern encapsulators are capable of filling combination products, such as mini-tablets with different release profiles (ER component and IR component) of same drug, or different types of mini-tablets, or mini-tablets combined with pellets or powder.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 2 Mar-Apr 2024, pp: 1766-1773 www.ijprajournal.com ISSN: 2249-7781

| Capsule Size | Number of Mini-tablets filled |
|---|---|
| 0 | 105 |
| 0 | 75 |
| 0 | 50 |
| 1 | 30 |
| 2 | 20 |
| 3 | 15 |
| 4 | 10 |

Table 03: Total number of mini-tablets filled based on capsules size

**VIII. Unit-dose packing of mini-tablets:**

Unit-dose packaging of mini-tablets has been receiving attention recently, especially for pediatric formulations. The unit-dose packaging can be referred to as stick-packs or sachets depending on the fill volume: stick-packs have smaller fill volumes, whereas sachets have larger fill volumes. The main advantage of unit-dose packaging is that it is suitable for packaging relatively large numbers of mini-tablets which can be beneficial for high dose drugs. With increasing complexity, more options can be included, such as an increased number of minitablets per dose, or the possibility of dispensing two or more products simultaneously.

Stick packing requires specific equipment and there are a number of stick packing machines available. They usually work on same vertical intermittent-motion principle. Specifically, a packaging machine such as the SBL-50 from Merz System is a vertically operating, fully automatic forming-, filling- and sealing machine for the production of very small tubular bags, referred to here as “Stickpacks”.

During stick packing, the machine processes flexible composite films (often including foil) from the flat laminate reel, cut lengthwise, formed to a tube during transportation and sealed lengthwise. It is then filled, sealed transversally, and cut. At the same time, photocell control assures the exact positioning of the print. The filling of stickpacks is dependent on multiple factors including the size of the dose, type of laminate/ sachet material, and the type of adhesive/polymer used to seal the sachet. In early process optimization, supplier recommended sealing criteria of the laminate/sachet material can be used but eventually critical process parameters need to be identified and then the range has to be established through development work.

Figure 03: Capsule filling machine

The critical process parameters related to stick packing are sealing temperature, sealing pressure; sealing dwell time and size of the stick pack which depends on fill volume. There is change parts required depending on the selection of products meaning powder dosing vs. mini-tablets dosing. In case of mini-tablets dosing, specifically fabricated dosing disk selected based on number of counts of mini-tablets per stick packs. By means of air pressure or vacuum, mini-tablets are removed from the dosing disk. The physical characteristics of mini-tablets such as thickness, length, width, diameter, diagonal length are very critical while ordering a dosing disk. With increasing complexity, more options can be included, such as an increased number of mini-tablets per dose, or the possibility of dispensing two or even more products simultaneously. Conclusion Mini-tablets present a promising alternative to liquid formulations administered to children of different age groups. Additionally, minitablets offer the advantage of combination therapy that it is not easily achievable with conventional tablets or capsules. In contrast, difficulty may also be encountered when designing a mini-tablet based dosage form because mini-tablets can be more easily dropped or lost relative to larger tablets but these risks can be mitigated through the appropriate choice of packaging configurations. Due to their unique size, some adjustments to the manufacturing process steps may be needed. The earlier development work related to flow property assessment can provide useful insights to help guide the development efforts. The manufacturing process typically involves unit operations such as dry or wet granulation to improve flow properties,

compression using multi tip tooling, Würster or pan coating, and encapsulation or stick packing. These manufacturing processes have a number of technological challenges when producing mini-tablets when compared to conventional tablets but careful evaluation of each unit operation can produce a better suited and robust mini-tablets based dosage form. As such, mini-tablets seem best implemented for small volume, high value products, particularly for pediatric patient populations that would benefit by this unique dosage form.

**Acknowledgements:**
I would like to thank Dr. A.P. Gorle, Head of the department of pharmaceutical technology, R.C. patel institute of pharmaceutical education and research, Shirpur, dhule, maharashtra. for their technical input and discussions in preparing this review paper.

## REFERENCES

[1]. Aleksovski A, Dreu R, Gasperlin M, Planinsek O (2015) Mini-tablets: A contemporary system for oral drug delivery in targeted patient groups. Expert Opin Drug Deliv 12: 65-84.
[2]. Breitkreutz J, Wessel T, Boos J (1999) Dosage forms for peroral administration to children. Paediatr Perinat Drug Ther 3: 25-33.
[3]. Breitkreutz J, Boos J (2007) Paediatric and geriatric drug delivery. Expert Opin Drug Deliv 4: 37-45.
[4]. Cram A, Breitkreutz J, Desset-Brethes S, Nun T, Tuleu C (2009) Challenges of developing palatable oral paediatric formulations. Int J Pharm 365: 1-3.
[5]. Bowles A, Keane J, Ernest T, Clapham D, Tuleu C (2010) Specific aspects of gastro-intestinal transit in children for drug delivery design. Int J Pharm 395: 37-43.
[6]. Ernest TB, Elder DP, Martini LG, Roberts M, Ford JL (2007) Developing pediatric medicines: identifying the needs and recognizing the challenges. J Pharm Pharmacol 59: 1043-1055.
[7]. Thomson SA, Tuleu C, Wong IC, Keady S, Pitt KG, et al. (2009) Minitablets: new modality to deliver medicines to preschool-aged children. Pediatrics 123: 235-238.
[8]. Spomer N, Klingmann V, Stoltenberg I, Lerch C, Meissner T, et al. (2012) Acceptance of uncoated mini-tablets in young children: results from a prospective exploratory cross-over study. Arch Dis Child 97: 283-286.
[9]. Stoltenberg I, Winzenburg G, Breitkreutz J (2011) Solid oral dosage forms for children-formulations, excipients and acceptance issues. Eur Ind Pharm 8: 4-7.
[10]. Lennartz P, Mielck JB (1998) Minitabletting: improving the compactibility of paracetamol powder mixtures. Int J Pharm 173: 75-85.
[11]. Tissen C, Woertz K, Breitkreutz J, Kleinebudde P (2011) Development of minitablets with 1 mm and 2 mm diameter. Int J Pharm 416: 164-170.
[12]. Guidance for Industry: Size of Beads in Drug Products Labeled for Sprinkle (2012) US Department of Health and Human Services FDA, Center for Drug Evaluation and Research.
[13]. Butler J, Cumming I, Brown J, Wilding I, Devane JG (1998) A novel multiunit controlled-release system. Pharm Tech, pp: 122-138.
[14]. Li YH, Zhu JB (2004) Modulation of combined-release behaviours from a novel “tablets in capsule system”. J Contr Rel 95: 381-389.
[15]. Ishida M, Abe K, Hashizume M, Kawamura M (2008) A novel approach to sustained pseudoephedrine release: differentially coated mini-tablets in HPMC capsules. Int J Pharm 359: 46-52.
[16]. Stoltenberg I, Breitkreutz J (2011) Orally disintegrating mini-tablets (ODMTs) - A novel solid oral dosage form for paediatric use. Eur J Pharm BioPharma 78: 462-469.
[17]. Riis T, Bauer-Brandl A, Wagner T, Kranz H (2007) pH-independent drug release of an extremely poorly soluble weakly acidic drug from multiparticulate extended-release formulations. Eur J Pharm Biopharm 65: 78-84.
[18]. Flemming J, Mielck JB (1995) Requirements for the production of micro tablets: Suitability of direct-compression excipients estimated from powder characteristics and flow rates. Drug Dev Ind Pharm 21: 2239-2251.
[19]. Flemming J, Mielck J (1996) Experimental micro tabletting: construction of an instrumented punch

holder for an eccentric tabletting machine. Eur J Biopharm 42: 212-214.

[20]. Shah N, Mehta T, Aware R, Shetty V (2017) Investigation on influence of Wurster coating process parameters for development of delayed release minitablets of Naproxen. Drug Development and Industrial Pharmacy.

[21]. Vuong H, Levina M, Rajabi-Siahboomi AR (2008) Investigation of enteric coating of mini-tabs using a perforated pan or a fluid-bed machine. 35th Annual Meeting and Exposition of the Controlled Release Society, New York, NY, USA.

[22]. Porter SC, Bubb G, Mehra DK, Sedlock R (2002) Modified-release matrix tablets coated with a modified-release film coating: Comparison of regular tablets with mini-tablets as an alternative to pellets. AAPS Annual Meeting and Exposition, Toronto, Canada.

[23]. Vuong H, Levina M, Rajabi-Siahboomi AR (2008) Evaluation of the Enteric Performance of Lansoprazole Mini-Tablets Coated in a Perforated Pan. AAPS Annual Meeting and Exposition, Atlanta, GA, USA.

[24]. Munday DL (1994) A comparison of the dissolution characteristics of theophylline from film coated granules and mini-tablets. Drug Dev Ind Pharm 20: 2369-2379.

[25]. Funaro C, Mondelli G, Passerini N, Albertini B (2010) Minitablets coated in a solid-wall pan for theophylline sustained-release capsules. Pharm Tech, pp: 38-42.

[26]. George S (2010) Atomic layer deposition: an overview. Chem Rev 110: 111- 131.

[27]. Hautala J, Kääriäinen T, Hoppu P, Kemell M, Heinämäki J, et al. (2017) Atomic Layer Deposition - A Novel Method for the Ultrathin Coating of Minitablets. International Journal of Pharmaceutics 531: 47-58.

[28]. Lopes CM, Sousa Lobo JM, Pinto JF, Costa P (2006) Compressed minitablets as a biphasic delivery system. Int J Pharm 323: 93-100.

[29]. Mitra B, Chang J, Wu SJ, Wolfe CN, Ternik RL, et al. (2017) Feasibility of minitablets as a flexible drug delivery tool. International Journal of Pharmaceutics 525: 149-159.

[30]. Alfred CFR, David H, Francis F, Varsha B, Mary AJ, et al. (2016) Minitablets: Manufacturing, Characterization Methods, and Future Opportunities. American Pharmaceutical Review