

**REVIEW ARTICLE**

# Recent Advancements in Tablet Technology: The need of hour

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**Abstract:** In this era of innovation and advancement in drug delivery for better clinical effects conventional dosages form have still a strong grip and most popular in all kinds of medicinal preparation intended for oral use. To satisfy the need of growing market tablets dosages form have incorporated automation in manufacturing and some advanced tablet types. Modified release tablet formulations including, layered tablets such as In-lay tablet, Bi-layered tablet, Medicated chewing gum, Tablet tarts, Pastilles, Lollipop, Tablet inserts, Clinicaps, Caplets, Child ecstasy tablet and Tablet in tablet are new entries in pharmaceutical market. This review highlights the current advancements and patents in tablet technology

**Keywords:** Tablet in Tablet, Layered Tablets, Caplets

## INTRODUCTION:

In recent decades, different pharmaceutical research has been conducted to develop new dosage forms which aim to enhance safety and efficacy and convenient dosage to achieve better patient compliance. Oral route of drug delivery is the most widely utilized route of administration among all the routes for the systemic delivery of drugs. The main goal drug delivery system is to provide the therapeutic amount of the drug at the site of action as an effective throughout the whole period of therapy and then maintain the desired drug concentration. The conventional dosage form produces a wide range of variation in drug concentration in the blood stream and body tissues which leads to reduction of drug effectiveness or increased incidence of side effects with subsequent undesirable toxicity and poor efficiency. The recent advance-

ments in tablet formulations include immediate release tablets such as orally dispersible mini tablets, mouth dissolving/fast dissolving tablets, conventional effervescent, uncoated and film coated tablets etc. modified release tablet formulations including layered tablets such as in-lay tablets, tablet in tablet, bilayered tablet, medicated chewing gum, tablet tarts, pastilles, lollipop, tablet inserts, clinicaps, caplets and child ecstasy tablets.

## BI-LAYER TABLETS

Bilayer tablet is a new era for successful development of controlled release formulations that have various features to provide successful drug delivery. In the last decade, interest in developing a combination of two or more than two active pharmaceutical ingredients (API) in a single dosage form (Bi-layer tablet) has increased in the pharmaceutical industry, endorsing patient convenience and compliance. Bi-layer tablet can be a primary option to avoid the chemical incompatibilities occurs between APIs by physical separation, and to allow the development of different drug release profiles that are immediate release with extended release.<sup>1</sup> The primary objective of sustained release drug delivery is to provide the safety and to improve efficacy of drugs. Bi-layer tablet is suitable for the sequential release in combination of two drugs, for separation two incompatible substances and also for sustained release tablet having one layer is immediate release as an initial dose and second layer is maintenance dose as sustained release.<sup>2</sup>

## MINI-TABLETS

The main goal of any drug delivery system is to provide a therapeutic amount of drug to the target site in the body to achieve and maintain the desired concentration of drug at that particular site. Usually conventional dosage form results in wide range of fluctuation in drug concentration in the blood stream and body tissues with consequent undesirable toxicity which results in poor efficiency.

Due to factors such as repetitive dosing, unpredictable absorption and undesirable toxicity lead to the concept of controlled drug delivery system. The main aim of designing controlled drug delivery systems is to reduce the dosing frequency and to increase the effectiveness of the drug by localization at the specific site of action in body.

Mini-tablets are small tablets having diameter ranging between 1.0-3.0 mm. They are typically filled into a capsule or compressed into larger tablets and sometimes placed in sachets for easy administration.<sup>23-25</sup>

**Table 1:-Various Advancements in the field of Bilayer Tablets**

Drug(s)	Dosage form	Clinical significance	Method of preparation	Year	Ref.no.
Amoxicillin and potassium clavulanate	Bilayer tablets	Produce effect against microbial infections	Dry Granulation	2014	3
Atorvastatin and atenolol	Bilayer tablets	Treatment of hypertension and hypercholesterolemia	Direct compression	2014	4
Losartan Potassium	Bilayer tablets	Biphasic release profile	Direct compression	2014	5
Diclofenac Sodium, Paracetamol	Bilayer tablets	Effective in reducing pain	Wet Granulation	2013	6
Telmisartan and hydrochlorothiazide	Bilayer tablets	To minimize contact b/w hydrochlorothiazide and basic component of telmisartan	Direct compression	2013	7
Rifampicin and Isoniazid	Bilayer tablets	Treatment of Tuberculosis	Wet Granulation	2012	8
Metformin Hydrochloride and Glipizide	Bilayer tablets	Treatment of Diabetes	Direct compression	2011	9
Ibuprofen, Methocarbamol	Bilayer tablets	Produce synergistic effect in back pain	Wet Granulation	2010	10
Metoprolol succinate and Amlodipine Besilate	Bilayer tablets	Treatment of hypertension	Wet Granulation	2010	11
Propranolol Hydrochloride	Bilayer tablets	Bimodal drug release	Direct compression	2009	12

**Table2:-Current patents status of bilayer tablet technology –a glimpse**

Patent No.	Field of Invention	Drug Candidate	Year of Publication	Inventors	Ref. No.
US 2015/0037410 A1	Pharmaceutical composition of ranolazine and dronedarone	Ranolazine and dronedarone	2015	Gerber et al.	13
US 8,637,078 B2	Bilayer tablet comprising telmisartan and diuretic	Telmisartan and hydrochlorothiazide	2014	Nakatani et al.	14
US 8,741,345 B2	Modified release pharmaceutical compositions of dexlansoprazole	Dexlansoprazole	2014	Cifter et al.	15
US 8,535,715 B2	Bilayer tablet formulations	Metformin	2013	Abebe et al.	16
US 8,524,278 B2	Controlled release pharmaceutical formulations of nitazoxanide	Nitazoxanide	2013	Rossignol et al.	17
US 7,332,183 B2	Multilayer dosage form containing NSAIDs and triptans	Naproxen	2008	Plachetka et al.	18
US 2006/0141037 A1	Bilayer tablets of oxcarbazepine	Oxcarbazepine	2006	Mehta et al.	19
US2006/0110450A1	Bilayer tablet of telmisartan and amlodipine	Telmisartan and amlodipine	2006	Eisenreich et al.	20
US 2005/0220877 A1	Bilayer tablet comprising an antihistamine and a decongestant	Ibuprofen	2005	Patel et al.	21

**Table 3:-Commercially available top selling marketed bilayer tablets:**

Brand name	Active Pharmaceutical Ingredients (API)	Developer
Volise-m	Voglibose, Metformin hydrochloride	Ranbaxy laboratories Ltd.
Unistar	Rosuvastatin, Aspirin	Unichem laboratories Ltd.
Pioglu	Pioglitazone, Metformin hydrochloride	Emcure pharmaceutical Ltd.
Glimeto-MP	Glimepride, Pioglitazone	RPG life Sciences Ltd.
Alprax plus	Sertraline, Alprazolam	Torrent pharmaceuticals.
TRIOMUNE 30	Nevirapine, Lamivudine, Stavudine	Cipla Ltd.

**Table 4:-Mini-Tablets Available In Market.<sup>23, 24</sup>**

Generic names	Brand names	Clinical significance	Developer
Pancrelipase	Ultresa	Used in digestive disorder.	Aptalis Pharma
Olanzapine	Olanex	Treatment of schizophrenia.	Ranbaxy
Zafirlukast	Zuvair	Treatment of asthma.	Dr Reddy Laboratories Ltd
Donepezil	Donaz	Treatment of Alzheimer's disease.	Glenmark Pharmaceuticals
Prasugrel	Effient	Used in acute coronary syndrome.	Eli Lilly and company Ltd.
Vorapaxar	Zontivity	Use to prevent heart attacks and strokes.	Merck & co., Inc.

**Table 5:-Current Patents Status of Bilayer Tablet Technology –A Glimpse**

Patent No.	Field of Invention	Drug Candidate	Year of Publication	Inventors	Ref. No.
US20130129824 A1	Solid Drug Tablets For Implantable Drug Drug Delivery Devices	Aminoamide and aminoester	2013	Daniel et al.	26
EP2533766 A2	Pharmaceutical mini tablets for sustained release of flecainide acetate	Flecainide acetate	2012	Arroyo et al.	27
US 7,807,195 B2	Extended release formulation of Venlafaxine hydrochloride	Venlafaxine hydrochloride	2010	Bhattacharya et al.	28
US006149939A	Healthful Dissolvable Oral Tablets, And Mini-Bars	Pycnogenols, food supplements, soy proteins, herbs	2000	Strumor et al.	29
US006110494A	Cisapride mini-tablet formulations	Cisapride	2000	Clancy et al.	30

### MOUTH DISSOLVING TABLETS

Oral Disintegrating Tablets (ODT) are defined as "A solid dosage form that contain medicinal substances and which disintegrates quickly within a matter of seconds, when placed upon the tongue. Oral route of administration is the most popular route for the systemic effects due to its ease of ingestion of accurate dosage with pain avoidance, self-medication, and most important patient compliance. Fast disintegrating tablets are also named as Fast-dissolving tablet, Mouth-dissolving, Melt-in-mouth, Quick-dissolving, Rapid dissolve, Quick-disintegration, Orally disintegrating, Fast-melt, Oro dispersible, and Effervescent drug absorption system.

Fast dissolving tablet can be administered to the patients who cannot swallow tablet/capsule such as elderly, stroke

victim, bedridden patients etc. FDT can be administered without water, anywhere, any time. Beneficial in cases of motion sickness, coughing, sudden episodes of allergic attack where rapid onset of action required.<sup>31-33</sup>

Mouth dissolving tablets that are available in market along with their activity are Piroxicam (NSAIDs), Olanzapine (Psychotropic), Ondansetron (Antiemetic), Rofecoxib (NSAIDs), Donepezil (Anti-Alzheimer's), Zolmitriptan (Anti-migrain) etc.

Some of the patented inventions in this field include "Fast dissolving tablet" published by Abu-Izza et al. (2004), "Fast dissolving tablet and its production" contains active ingredient such as NSAIDs, Vitamins, Anti-Hypertensive Drug Etc. published by Kikuta et al. (2002) and Makino et al.

(1996).

**Table 6:-Commercially Available Fast Dissolving Tablets in Market** <sup>31-35</sup>

Brand name	Active ingredient	Application	Developer
Felden fast melt	Piroxicam	NSAIDs	Pfizer Inc., NY, USA
Zyprexa	Olanzapine	Psychotropic	Eli Lilly, Indianapolis, USA
Zofran ODT	Ondansetron	Antiemetic	Glaxo Wellcome, Middlesex, UK
Torrox MT	Rofecoxib	NSAIDs	Torrent
Aricept ODT	Donepezil	Anti-Alzheimer's	Eisai co.
Zomig-zmt and Rapimelt	Zolmitriptan	Anti-migrane	Astrazeneca alavert Loratadine allergy
Nulev	Hyoscyamine Sulfate	Anti- Ulcer	Schwarz Pharma
Claritin Reditabs	Loratadine	Antihistamine	Schering Corporation
Nimulid md	Nimusulide	NSAIDs	Panacea
Febrectol	Paracetamol	Antipyretic	Prographarm, Chateaufneuf, France
Olanex Instab	Olanzapine	Psychotropic	Ranbaxy lab. Ltd. New-Delhi, India

**Table 7:- Current patents status of fast dissolving tablet technology –a glimpse**

Patent No.	Field of Invention	Drug Candidate	Year of Publication	Inventors	Ref. No.
US 6,733,781 B2	Fast dissolving tablet	NSAIDS	2004	Abu-Izza et al.	36
EP 0553777 B1	Fast dissolving tablet and its production	NSAIDS, Vitamin ,Anti Hypertensive Drug Etc	2002	Kikuta et al.	37
US005501861 A	Fast dissolving tablet and its production	NSAIDS, Vitamine ,Anti Hypertensive Drug Etc	1996	Makino et al.	38

### INLAY TABLETS

Inlay tablet is a type of layered tablet in which instead the core tablet being completely surrounded by coating and the top surface is completely exposed. Tablet compression was done with core rod tooling in which drug is incorporated in cup portion and the other surface of the core is exposed to the outside. While preparing, only the bottom portion of the die cavity is filled with coating material and core is placed upon it. During the compression, some coating material is displaced to form sides and compresses the whole tablet. The main body portion may consist of uncoated granules which are compressed around the enteric coated inlay portion. In this modification of tablet the main body portion is first released and assimilated in the gastrointestinal tract while other the enteric coating protects the inlay portion of tablet for a predetermined period of time so as to provide time delayed or sustained medication.<sup>39-41</sup>

The present invention of inlay tablet also teaches the use of dual retard technique to effectively control the release rate of active ingredient by using small quantity of release controlling agents. Due to this dual retard technique the size of dosage form sufficiently reduces, which is convenient for swallowing.

#### Formulation of inlay tablet as listed below:<sup>40</sup>

- Atoz Inlay tablets with combinations like Metformin 500 mg sustained release and Pioglitazone 15 mg.
- Ursinos is the marketed inlay tablets containing aspirin.
- Rosiglitazone IR + Metformin SR Tablet (**TORRENT PHARMACEUTICALS**).
- Isoniazid And Salbutamol Sulphate Inlay Tablet<sup>39</sup>

#### Patented Inlay Tablet:<sup>40</sup>

- Pravastatin Sodium (10 mg) + Niacin (500 mg).

- Rosiglitazone Maleate (2 mg) + Metformin Hydrochloride (500 mg).
- Glimipride (2 mg) + Metformin Hydrochloride (500 mg).
- Lamotrigine (25 mg) + Sodium Valproate (500 mg).

### CAPLET

Dosage form of a drug is that which enters the body, reaches the site of action and exerts its action. Dosage forms of the drug is to be the most appropriate form for each route of administration. It should be characterized by various aspects according to the need of masking unpleasant odor and bad taste. The caplets are oval in shape. Caplet is a tablet like any other tablet, but should be differs only is being a smoothly-coated tablet shaped like an ordinary capsule.

Caplets are the oblong-shaped tablet, and to be used as an alternative to the capsule, and can be easy to swallow dosage form. So that it is used as alternative to a regular tablet. It could be considered as most convenient and commonly used dosage forms which is taken per os (via oral route), tablets and capsules.<sup>42</sup>

#### Caplet Products Available In Market:<sup>42</sup>

- Calci-D film coated caplets, used for patients with calcium deficiency. It is presented as blisters of 10 caplets.
- Paracetamol (Acetaminophen) Caplets, a well-known NSAID and used mainly as anti-inflammatory, antipyretic, analgesic, and for mild to moderate pains accompanied with cold and flu.
- Imodium caplets help to restore balance of your digestive system. The Imodium caplet controlling the symptoms of diarrhea, including Traveler's Diarrhea.
- Nurofen caplets (ibuprofen), they are used for targeted relief for pain.
- Excedrin migraine caplets, contain acetaminophen, aspirin, and Therapeutically Active Caffeine and are used for pain reliever.

### CLINICAPS

Clinicaps capsules are the two-piece gelatin capsules which are specially designed for studies of 'double blind' during clinical trials. After closure (locking), caps are closes tightly on the body and keeping only the dome of the body visible. After locking it is difficult to open the capsule that prevents tampering and effectively hides the sample. Clinicaps capsules are useful to encapsulate the tablet or capsule dosage form in the body and mask the placebo. This will ensures the integrity of the blind study of clinicaps and improves patient compliance. As wide is the diameter of clinicaps capsules that help to contain large diameter or unequally shaped tablets which helps to

eliminates the need of split or grind tablets. These capsules are shorter in length so as to enhance ease of swallowing them and are made for ease of use (Fig. 1). These are filled by mostly automatic, semi-automatic filling machines, and manual capsule filling machines.<sup>43</sup>

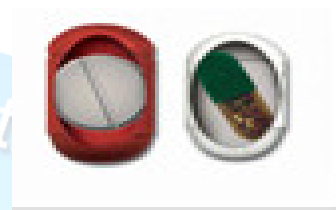


Fig. 1: - Clinicaps

### PASTILLES

A pastille is a form of sweet or medicinal pill made up of solidified thick liquid that meant to be consumed by light chewing and is allowing it to dissolve in the mouth. Pastilles are also used to define certain forms of incense. Pastille is also known as "Troche" and medicated lozenge that dissolve rapidly like candy.<sup>44</sup>

#### CHILD ECSTASY TABLET

3,4-methylenedioxy-methamphetamine (MDMA) a psychoactive drug of the substituted methylenedioxy-phenethylamine and amphetamine classes of drugs that is consumed mainly for its euphoric and empathogenic effects. Pharmacologically, MDMA can acts as a serotonin-norepinephrine-dopamine releasing agent and reuptake inhibitor.

MDMA is widely known as "Ecstasy", usually in its tablet form, although this term may also hold the presence of possible adulterants. MDMA in a crystalline powder form free of adulterants such as "mandy" as termed in the UK and "molly" as termed in the US.

In most countries Possession of MDMA is illegal. Some limited exceptions are exist for the scientific and medical research. MDMA may have health beneficial effects in certain mental disorders, but also has potential adverse effects that include neurotoxicity and cognitive impairment.<sup>45</sup>



Fig.2:- Child Ecstasy Tablets

### LOLLIPOP

Lollipops are sugar-based lozenges on a stick. Good for children. Also ideal for patients requiring breakthrough cancer pain medication who cannot swallow tablets or

capsules; provides almost immediate relief.<sup>46</sup>

#### GUMMY BEARS:

Gummy bears contain medication in a flavored gummy candy. Good for children.<sup>46</sup>

#### Conclusion:

With growing pharmaceutical market and needs of patients, newer developed tablets may satisfy the consumers. Advancement in Tablet manufacturing or some novel tablet modification has made strong presence in the market by their significant contribution. Formulation scientist across the globe are constantly working in this segment to provide better dosages form which is going ultimately to benefit the healthcare system.

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