International Journal of Medical and Health Research
ISSN: 2454-9142
Received: 12-11-2018; Accepted: 13-12-2018
www.medicalsciencejournal.com
Volume 5; Issue 1; January 2019; Page No. 84-91

Orally disintegrating tablets: A novel approach for medication

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Abstract
Orally disintegrating tablets (ODTs) are solid dosage forms designed to improve disintegration and dissolution rates of any pharmaceutical product. Orally disintegrating tablets are distinct from ordinary tablets in that they are intended to dissolve on the tongue rather than be swallowed. This article discusses the advantages of orally disintegrating tablets (ODTs) over conventional tablets, including ease of administration, convenience, and increased bioavailability, and to conclude the present and future of ODTs. ODTs are in ever-increasing demand, and this specific subject is a rapidly rising area in the pharmaceutical industry. When these tablets are introduced into the mouth, they dissolve or disintegrate in the absence of additional water. When ODTs are placed on the tongue, they rapidly disintegrate, releasing the medication, which dissolves or disperses in the saliva fluid. As saliva goes through the stomach, some medications are absorbed from the mouth, pharynx, and oesophagus. In such circumstances, the bioavailability of drugs is much higher than that observed with the traditional tablet dosage form. The benefits of this dosage forms are becoming more widely recognized in both industry and academics. Their expanding significance was recently highlighted when the European Pharmacopoeia introduced the term "Oro- dispersible Tablet" to describe a tablet that is to be placed in the mouth and dispersed swiftly before swallowing. ODTs have several challenges, and incorporating the usage of herbal substances would make it even more difficult, but solutions to these challenges are demonstrated in this study.

Keywords: orally disintegrating tablet, bioequivalence, limitations of ODTs

1. Introduction

Orally disintegrating tablets (ODTs) are solid dosage forms designed to improve disintegration and dissolution rates of any pharmaceutical product. The oral route of administration is the most preferred route of administration, and tablet and capsule dosage forms are the most preferred dosage forms; it is currently the gold standard in the pharmaceutical industry, where it is regarded as the safest, most convenient, and most economical method of drug delivery with the highest patient compliance; however, there are several limitations of that type of dosage form, such as chocking and swelling discomfort in geriatric and paediatric patients[1, 2, 3, 4]. The development of the orally disintegrating tablets and related new technologies compensate many pharmaceuticals and patients' needs, ranging from enhanced life-cycle management to convenient dosing for paediatric, geriatric, and psychiatric patients with dysphasia [5]. Over the past three decades, orally disintegrating tablets (ODTs) have gained considerable attention as a preferred alternative to conventional tablets and capsules due to the better patient compliance [6]. The other terms used for ODTs are orodispersible, rapid-dissolving, mouth-dissolving, rapid-disintegrating tablets. There are some definitions made by pharmacopoeias and other agencies: Orodispersible tablets have been placed in the mouth where they disperse fast before being swallowed and they are uncoated tablets. The average disintegration time of Orodispersible tablets is 180 seconds, when the disintegration tests have been conducted up to the test for disintegration of tablets [7, 8]. Orally disintegrating tablets are intended to disintegrate fast in the mouth to provide dispersion before being get swallowed, where the active ingredient is intended for gastrointestinal delivery and/or absorption [9, 10]. A solid dosage form contains active ingredients which usually disintegrate fast, usually within seconds, when put on the tongue. In addition to those definitions, FDA recommends that orally disintegrating tablets should be considered as solid oral preparations that get disintegrated fast in mouth, with an in-vitro disintegration time of approximately less than or equal to 30 seconds, when the disintegration test get conducted to the United States Pharmacopeia (USP) disintegration test method or other alternative [11, 12]. Products related to the ODT technologies entered the market in the 1980s, have grown steadily in demand, and their product pipelines are rapidly expanding [6]. For the past one decade, there has been an enhanced demand for the patient-friendly and more compliant dosage forms. As a result, the demand for developing new technologies has been increasing day by day [13]. The Catalent Pharma Solutions (formerly Scherer DDS) in UK, Cima Labs in the US and Takeda Pharmaceutical Company in Japan are some of the initiators for the development of the ODTs. The first ODT which got the approval from the US Food and Drug Administration (FDA) was Zydis ODT formation of Claritin (loratadine) in December 1996. It was followed by Zydis ODT formulation of Klonopin (clonazepam) in December 1997, and a Zydis ODT formulation of Maxalt (rizatriptan) in June 1998 [14]. The clinical categories having greatest potential for ODTs about 92% of the ODT world market is in the three therapeutic categories (2004). These are Central nervous system having 50% of market share, Gastrointestinal having 29 % of market share and Oncology having a 13% of market share. Drugs with the greatest potential for success with ODTs are treatments for gastro oesophageal reflux disease (GERD), pain, schizophrenia and other central nervous system (CNS) diseases, Parkinson's disease, nausea, migraine and sleeping aids [15]. The global ODT market (based on ex-factory sales to wholesalers) was estimated at $2.4 billion in the year of 2004 according to Technology Catalysts International [16].

Number of new consumer health and prescription product launches in recent years, the ODT market was predicted to easily reach $3 billion in 2006, including brands and generics. The market continues to grow at the rate of 20% each year, with a growing penetration of the generic ODTs. The oral drug delivery market was estimated to be worth $35 billion in 2006 & forecast to reach $52 billion by 2010 with a CAGR of 10%. The ODT, taste masked & micro emulsion formulation segments constitute a good share (22%) with an expected CAGR of 17% to 2010. There is a clear opportunity for the new enhanced oral products which arise within this market segment [17-21]. Looking at the recent years sales figures of some ODTs in the world, for 2013, Zomig and Zomig-ZMT tablets garnered annual sales of $ 176 million [22] and Orapred ODTs has $ 33 million in estimated U.S. sales figure for 2014 [23]. Additionally, we can give some os the sales figure for Turkey. Sales figure of the Zofran ODTs was almost $ 1.4 million in the year of 2013 whereas, in 2014 it was almost $ 1.5 million. Also the sales figure of Maxalt ODTs in the year 2014 was almost $ 1.7 million [24]. After defining the ODT and giving some market information about ODTs this article is not envisioned to offer a comprehensive review on ODTs but to highlight the BE studies, some of the recent situation regarding the formulation development, patent etc. in this field.

***In vivo* biological equivalence**

Biological equivalence of ODTs has some challenges but in this part basic solutions to overcome these challenges were given. Active pharmaceutical ingredients that are been formulated as the ODTs should be dispersed or dissolved in the saliva, then directly absorbed via oral mucosa and/or absorbed through the gastrointestinal system. When defining the dissolution test conditions to prove both of the in-vitro and in-vivo bioequivalence of two formulations, the physiological conditions of the mouth should be considered in that case. Flow rate, pH, volume of the saliva and targeted population are the important factors that should be considered. For ODTs there are several in-vivo studies that are conducted to prove bioequivalence of the ODTs, nevertheless BCS based biowaiver is also being considered for especially the active pharmaceutical ingredients are not been absorbed via oral mucosa, but are absorbed through the gastrointestinal system. But if it cannot be demonstrated, bioequivalence must be evaluated through in-vivo studies [25]. If bioequivalence between oro-dispersible table taken without water and the reference formulation with water is demonstrated in a two-period study, bioequivalence of ODT taken with water can be assumed. However, if the oro-dispersible tablet's test product is an extension to another oral formulation, a 3-period study is recommended in order to evaluate administration of the oro-dispersible tablet both with and without concomitant fluid intake. If the ODT is a generic/hybrid to an approved oro-dispersible tablet reference medicinal product, the following recommendations regarding study design apply:

- If the substance may be dissolved and partly absorbed in the oral cavity denoting the reference medicinal product can be taken with or without water hence bioequivalence should be demonstrated without the presence of water, as this condition best resembles the intended use of the formulation. This is especially important if bioequivalence is demonstrated when taken without water, also bioequivalence can be assumed with ODT taken with water.
- If it is taken only with water, bioequivalence should be shown in a conventional two-way crossover design
- If it is taken only with water, and the test product is intended for additional ways of administration without water, the conventional and the new method should be compared with the reference in the conventional way of the administration (3 treatment, 3 period, 6 sequence design).

In studies evaluating ODTs without water, it is to be recommended to wet the mouth by swallowing 20 ml of water directly before applying the ODT on the tongue. It is recommended not to allow fluid intake earlier than 1 hour after its administration. Other oral formulations such as buccal tablets, orodispersible films, sublingual tablets and chewable tablets may be handled in a similar way as for the oro-dispersible tablets. Bioequivalence studies should be conducted according to the recommended use of the target product [26].

It would seem appropriate that the solubility criterion should be amended accordingly as the BCS biowaiver is based on the intake of the tablet with a glass of water (i.e., solubility in 250 ml) and the orodispersible tablets are usually taken without water, The parameters of the dissolution method especially volume of the saliva to characterize ODTs that simulate oral cavity have not yet been developed. It is noteworthy that, the demonstration of bioequivalence without the water is considered the worst case scenario and it is assumed that the formulation will be also equivalent with concomitant intake of water. However, such an assumption is questionable when either the test or the reference of the orodispersible tablet contains mannitol since the presence of water might increase the differences in absorption due to the osmotic effect of the mannitol present in it [27].

The Biopharmaceutical classification system (BCS)-Biowaiver scheme (BWS) can be expanded to BCS class III drugs and ODTs. Whereas, for the BCS class III drugs with a relatively high dose to solubility ratio, it is possible that the discrepancy of the in vitro dissolution profiles does not necessarily translate to the bioequivalence in-vivo. The results of this study which includes the dissolution studies at pH 1.2 and pH 6.8 of 6 active pharmaceutical ingredients, suggest that extension of the BCS-BWS to oral dispersible tablets and immediate release formulations of BCS class III drugs is appropriate. Whereas, for the BCS class III drugs with a relatively high dose to solubility ratio, clinical bioequivalence would be achievable even if when two formulations showed different dissolution profiles in vitro. [28].

The EMA guideline states that the biowaivers are only applicable when comparing products with the same dosage form. In the case of oral dispersible tablets, the product might be considered for a BCS-based biowaiver, which does not mean that it is actually possible, because it is not known how to define the volume of water for the solubility classification and the current dissolution methodology is also questionable for a product that is going to be dispersed in the mouth without the intake of a water. In the most optimistic case,

BCS-based biowaivers of ODTs would be acceptable only if thereis a test ODT and a reference ODT, not with different immediate release formulations and the solubility classifications should consider the administration instructions of the reference product, which should be identical for the test product [29]. The clinical study was designed as an open-label, single-dose, randomized sequence, 2-period crossover study. Healthy and the non-smoking Chinese male volunteers were randomly assigned to receive a 150 mg (administered as three 50-mg tablets) of either the test or reference formulation of flurbiprofen, followed by a 7-day wash-out period and administration of the alternate formulation of the same. Test drugs were administered after a 12-hour overnight fasting. Blood samples were collected before dosing and at a time interval of 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, 8, 12, and 24 hours after dosing. This single-dose study of flurbiprofen-150 mg (three 50-mg tablets of each formulation) found that the test (flurbiprofen 50-mg ODT) and the reference (flurbiprofen conventional 50-mg tablet) products met the regulatory criteria for the bioequivalence in these fasting healthy Chinese male volunteers. Both formulations were generally been well tolerated [30].

Other example includes a total of 427 cancer patients receiving cyclophosphamide chemotherapy participated in this multicenter, double-masked, double-dummy, parallel-group, randomized study comparing the antiemetic efficacy and safety of an 8 mg conventional ondansetron tablet taken twice daily with an 8 mg orally disintegrating ondansetron tablet taken twice daily for 3 days. In the primary efficacy analysis the complete or major control of emesis between days 1 and 3 was seen in 80% of OT and 78% of oral dispersible tablet patients. ODT provides greater choice and flexibility in the management of the emesis and nausea. Oral dispersible tablet and OT, 8 mg given twice daily for 3 days are both well tolerated and are of equivalent efficacy in preventing the cyclophosphamide-induced nausea and vomiting. Oral dispersible tablet hence represents an easy-to-administer, palatable, well-tolerated, and effective alternative to OT for cancer patients. It may be particularly useful in an ambulatory setting and is likely prove to be beneficiary in patients who have difficulty swallowing a conventional tablet [31]. In an another study a total of 23 healthy volunteers, 12 males and 11 females, participated in the study after signing a consent form. The subjects had mean age of 30 years, mean body weight of 64 kg, and a mean height of 1.66 m. The subjects with a history of drug allergies, renal or hepatic impairment, history of any illness of cardiovascular system, or alcohol and drug abuse were excluded. The subjects were selected after a clinical screening procedure including a physical examination and laboratory tests. All the subjects avoided using other drugs for at least one week prior to the study and until after completion of it. They also been abstained from taking alcoholic beverages, xanthine-containing foods and beverages 48 h prior to each dosing and until the collection of the last blood sample. The study was an open, randomized, two-period crossover trial with a one week washout period. The subjects were admitted to the hospital at 7 p.m., the day before the study has been taken and fasted 10 h before each drug administration. An 8 mg single dose consisting of one Vonau® flash or Zofran® tablet according to the randomization plan was given to each of the subject in the fasting state for each treatment period. Fasting continued for four more hours after the drug administration. The drug was administered with 240ml of the water. Subjects were fed with the standard meals 4 h (lunch), 7 h (snack) and 10 h (supper) after the drug administration in each of the treatment. The 90% confidence intervals for AUC_{0-t} (89.3–107.2%), AUC0–∞ (89.7–106.0%) and C max (87.5–103.8%) are within the 80–125% interval, proposed through most regulatory agencies (FDA, EMEA, ANVISA). It was concluded that the two formulations are bioequivalent in their rate and in their extent of absorption and thus, may be used interchangeably, without any prejudice of therapeutic effect [32].

Formulation Development of ODTs

The most important parameters to formulate ODTs is the selection of active pharmaceutical ingredient. It should be dissolved in the oral cavity and absorbed. Also it shouldn't have bitter taste. It's good if it is of low dose, small to moderate molecular weight, good solubility in water and/or saliva, non-ionized property in pH 5.5-7.4 and ability to be absorbed via oral mucosa. In the formulation development of oral dispersible tablets, excipient selection is important for disintegrating the tablet immediately and also important for masking bitter taste. The main excipient groups are diluents, disintegrants (disintegrate mechanisms), flavors, and taste masking agents, sweeteners, binders, lyoprotectans, glidants and lubricants. To achieve the challenges, more specific excipients can be used in different ranges.

The selection of Excipients is as important asthe selection of manufacturing method. Because different technologies have various positives and negatives. Some of those methods are patented. Those patented technologies are ORASOLV®, WOWTAB®, DURASOLV® EFVDAS®, FLASHTAB® (main approach is conventional tablet processes with modifications), ZYDIS®, LYOC®, QUICKSOLV® (main approach is freeze drying method) and FLASHDOSE® (main approach is floss formation).

In the Table, some marketed ODTs and their manufacturing technologies, and major advantages were given [33-40].

Table 1

Manufacturing Technology	Active Ingredient	Brand Name	Category	Technological basis	Advantages
Zydis®	Loratadine	Claritin	Antihistaminic	Lyophilization	Very fast disintegration (2-10 s)
Orasolv®	Mirtazapine	Remeron	Antidepressant	Compressed tablets	Effervescent disintegration
Zydis®	Olanzapine	Zyprexa	Antipsychotic; Serotonin-Dopamine Antagonist	Lyophilization	Very fast disintegration (2-10 s)
Zydis®	Ondansetron	Zofran ODT	Nootropic; Antiemetic; Serotonin Receptor Antagonist	Lyophilization	Very fast disintegration (2-10 s)
Zydis®	Risperidone	Risperdal	Antipsychotic; Dopamine Receptor Antagonist; Serotonin Dopamine Antagonist	Lyophilization	Very fast disintegration (2-10 s)

Zydis®	Rizatriptan	Maxalt	Antimigraine; Serotonin Receptor Agonist	Lyophilization	Very fast disintegration (2-10 s)
Flash Dose®	Tramadol	Ultram	Analgesic (Non-narcotic)	Cotton Candy Process	Effectively taste masking
Dura Solv®	Zolmitriptan	Zomig	Antimigraine; Serotonin Receptor Agonist	Compressed tablets	Easy to formulate low dose of active ingredient and higher mechanical strength than Orasolv
Flash Dose®	Zolpidem	Ambien	Sedative/Hypnotic	Cotton Candy Process	Effectively taste masking

More recent innovator system called 'SeDeM-ODT' can be mentioned as an accessorily to the selection of excipients, that can be used in direct compression manufacturing method. 'SeDeM-ODT' is a new and based on an earlier SeDeM expert systems that provide to predict compliance of powder blend which produce immediate release tablets by direct compression. This expert system has one of the major advantages i.e. it avoids application of unnecessary inactive ingredients [41].

The most preferred manufacturing method to produce ODTs is direct compression. Using 'SeDeM-ODT' expert system, many of the excipients can be evaluated. The 'SeDeM-ODT' expert system has 12 parameters such as bulk density, tapped density, inter-particle porosity, Carr index, cohesion index, Hausner ratio, angle of repose, powder flow, loss on drying, hygroscopicity, particle size, homogeneity index, which can be classified into 5 factors (compressibility, flowability/powder flow, dimensions, lubricity/stability, lubricity/dosage) to determine the index of good compression (IGC). That complies to analyse the suitability of 43 excipients for direct compression manufacturing method [42, 43, 44].

Table 2: ODT technology: Patented and Recent advancements

Patented technology	Novelty	Handling / storage of dosage form	Release of Drug
Orasolv (CIMA LABS, INC.)	Its Unique taste masking, The Effervescent disintegrant used, Light compression.	The tablets were soft and fragile, so needed to be packed in specially designed pick and place package systems.	The Disintegration time was in 5-45 sec depending upon the size of the tablet, No significant change was observed in drug bioavailability.
Durasolv (CIMA LABS, INC.)	It's similar to the Orasolv, but with a better mechanical strength.	Packaged in the blisters or foil or bottles with good mechanical strength.	The Disintegration time was in 5-45 sec, No significant change was observed in drug bioavailability.
Wowtab (Yamanouchi Pharma Technologies, INC.)	They are Compression moulded tablets with proprietary taste masking.	Avoid exposure to the moisture or humidity, packed into the bottles and/or blister packs.	The Disintegration time was in 15 sec or less depending upon the size of the tablet, No significant change was observed in drug bioavailability.
Flashtab (Prographarm group)	It's a Compressed dosage form, drug as microcrystal.	Only conventional tableting technology is required for it.	It get dissolved in 1 min.
Flashdose (Fuisz Technologies, LTD.)	Its Unique spinning mechanism producing the floss-like crystalline structure as cotton candy.	Avoid exposure to the Moisture and humidity and Require specialized Packaging.	It get dissolved in 1 min., with enhanced bioavailability

Some tests are conducted to prove the quality of ODTs. But the most critical tests includes disintegration and dissolution to prove in-vitro equivalence of the formulation. There are some more compendial and non-compendial methods for the disintegration test and there are also different limitations for those tests. The Frequent disintegration tests can also be conducted to USP current edition. The Dissolution tests are usually being conducted at the pH of 1.2 and pH of 6.8 to simulate the oral and pregastric absorption. But sometimes different the mediums can be chosen up to the APIs pKa.

Patented Technologies: Advantages and Disadvantages [5, 6]

Table 3

Technique	Advantages	Disadvantages
ZYDIS	Quick dissolution, self-preserving, increased bioavailability	Expensive process, poor stability at higher temperature and humidity's.
Orasolv	Its taste masking is twofold, quick dissolution takes place	Have low mechanical strength.
Durasolv	Higher mechanical strength than Orasolv, good rigidity	Inappropriate with larger doses.
Wowtab	Adequate dissolution rate and hardness.	No significant change in bioavailability.
Flashdose	It have a high surface area for dissolution	It require a high temperature required to melt the matrix can limit the use of heat sensitive drugs, it's sensitive to moisture and humidity.
Flashtab	It require only conventional tableting technology.	-
Ziplet	Good mechanical strength, handling problems during manufacturing are avoided, satisfactory properties can be obtained at high dose (450 mg) and high weight (850 mg)	As soluble component dissolves, the rate of water diffusion in to the tablet is decreased because of the formation of viscous concentrated solution.
Oraquick	Faster and efficient production, appropriate for heat-sensitive drugs	-

Advantages of ODTs

ODT formulation combines the advantages of both liquid and conventional tablet formulations which is its major advantage. Convenience of a tablet formulation is provided, and also allows the ease of swallowing as like liquid formulation.

Others are

- Easy dissolution or disintegration in saliva within a few seconds.
- Requirement of water or other liquids for swallowing is not needed.
- No residue in the mouth when administered.
- Accurate dosing if compared with liquids.
- Can be manufactured by direct compression method with low cost.
- It is easily administrable to children, old and mentally disabled patients.
- Offering rapid onset of action due to fast dissolution and absorption of drug.
- Some drugs are absorbed from mouth, pharynx and oesophagus through saliva transferring down into the stomach hence bioavailability of drug is increased.
- Offering improved bioavailability by reducing first pass metabolism and thus reduces dose and side effects.
- Offering improved safety by nullifying the risk of suffocation due to physical obstruction when swallowed.
- Best suited for sustained/controlled release actives.
- High drug loading is observed [45-52].

ODTs: Challenges and Limitations

- Relatively larger doses drugs are difficult to formulate into ODTs e.g. the antibiotics such as ciprofloxacin (adult dose) tablet containing about 500 mg of the drug [53].
  The applicability of technologies used for ODTs is limited by the amount of drug into each unit dose. The dose of the drug must be lower than 400mg for insoluble drugs and 60mg for soluble drugs [54].
  Whereas Flashdose technology can accommodate larger drug doses hence offering improved mechanical strength. The Orasolv® technology can accommodate a wide range of active pharmaceutical ingredient ranging from 1 mg to 500 mg [38].
- The Mechanical strength – Oral dispersible tablets are made of the porous or soft molded matrices in order to allow its disintegration into the mouth. This makes the tablet friable hence handling of it becomes difficult.
  By the use of sublimation methodorodispersible tablets with highly porous structure and good mechanical strength have been developed. Also the Durasolv® has much higher mechanical strength than the Orasolv due to the use of higher compaction pressures during the compression process.
- The Palatability - Oral dispersible tablets are intended to be dissolved in mouth. Most of the drugs have bitter taste. Bitter taste can be masked with enough sweeteners and flavours to be incorporated in it. Most probably methods of taste masking include lipophilic vehicles, coating with polymers, carbohydrates, lipids or proteins complexation with cyclodextrins or ion-exchange resins, formation of salts, use of salting out layers and solid dispersions [55].
  OraQuick applies its own patented taste masking technology i.e. MicroMask®. In MicroMask® technology, taste masking process is done by incorporating drug into matrix microsphere [56].
- Drugs in form of ODTs are hygroscopic in nature therefore need to be protected from humidity.
  For overcoming the problem of humidity special working facilities can be designed by simple methods and special air-conditioning systems can be set up. Size of tablet 7 and 8 mm are easy to swallow while tablets of size 8mm are easy to handle. Hence sizes of the tablets which are both easy to handle and swallow are difficult to be achieved. To make the swallowing easier, round shape punches having optimum dimensions can be used for the patient compliance.
- Drug candidates must be stable both in water and in saliva, should not ionize at oral cavity pH and should be able to permeate oral mucosal tissue to diffuse and partition in the upper gastro intestinal epithelium (logP > 1, or preferably > 2, not have short half-life). To optimize the solubility problem of an active pharmaceutical ingredient some solid buffers and the surfactants can also be chosen.
- For proper stabilization and safety of stable product ODTs requires special packaging [40, 41].

Herbal tablets available in Market

Following are some herbal tablets available in the market which can be formulated as ODT:

Table 4

Active ingredient/ Brand name	Scientific name	Formulation	Manufacturing company
Ashwagandha	Withania somnifera	Tablet	Banyan botanicals
Shatavari	Asparagus racemosus	Tablet	Banyan botanicals
Kanchanar Guggulu	Bauhinia variegate Commiphora mukul	Tablet	Banyan botanicals
Turmeric	Curcuma longa	Tablet	Banyan botanicals
Mandukaparni (Gotu-kola)	Centellaasiatica	Tablet	Himalaya Herbals
Arjuna	Terminelia Arjun	Tablet	Himalaya Herbals
Amalaki	Emblica officinalis	Tablet	Banyan botanicals
Haritaki	Terminalia chebula	Tablet	Banyan botanicals
Neem	Azadirachta indica	Tablet	Banyan botanicals

Number of formulations are made by using mixed ingredients for different purposes. Following are some of the herbal tablet preparations which are available in the market containing more than two ingredients which can be implemented for making herbal ODTs:

Table 5

Brand name	Ingredients	Formulation	Manufacturing company
Blood cleanse	Manjistha, Neem, Turmeric, Guduchi, Burdock	Tablet	Banyan Botanicals
Everyday greens	Spirulina, Alfalfa, Barley, Wheat, Oat, Dandelion Greens	Tablet	Banyan Botanicals
Meryton	Ashoka, Shatavari, Guduchi	Tablet	Vasu Healthcare
GokshuradiGuggulu	Gokshura, Guggulu, Musta, Amalaki, Bibhitaki, Haritaki, Pippali, Ginger, Black pepper	Tablet	Banyan Botanicals
Equiline	Valerianawallichii, Withaniasomnifera, Asparagus racemsus, Emblicaofficinalis, Terminaliachebula, Convolvulus pluricaulis, Centellaasiatica	Tablet	JivaAyurvedic Pharmacy Ltd.
Healthy bones	Coral, Arjuna, Ashwagandha, Ginger	Tablet	Banyan Botanicals
Step	Guduchi, Tulsi, Haldi	Tablet	Vasu Healthcare
Healthy Hair	Bhringaraj, Amalaki, Brahmi, Hibiscus,	Tablet	Banyan Botanicals
Healthy Kapha	Bibhitaki, Chitrak, Punarnava, Tulsi, Turmeric, Bhumayamalaki, Ginger, Pippali	Tablet	Banyan Botanicals
Jambruyog	Jambugiri, Shilajeet, Mamejava, Bilipatra, Gudmar, Nimpatra, Karela, Methi, YasadBhasma, Bang Bhasma.	Tablet	UnjhaAyurvedic Pharmacy
Healthy Pitta	Brahmi, Bhringaraj, Guduchi, Shatavari, Manjista, Bhumayamalaki, Fennel	Tablet	Banyan Botanicals
Skin Fit	Anantmul, Manjista, Neem, Turmeric, Brahmi/Gotu-kola, Guduchi,	Tablet	JivaAyurvedic Pharmacy Ltd.
Immune support	Licorice, Kalmegh, Pippali, Turmeric, Ginger, Amalaki, Bibhitaki, Haritaki, Cardamom	Tablet	Banyan Botanicals
Healthy Heart	Arjuna, Purnarnava, Guduchi, Hawthorn berry, Brahmi, Amalaki, Bibhitaki, Haritaki, Guggulu, Pippali, Ginger,	Tablet	Banyan Botanicals
Diarrinol	Holarrhenaantidysenterica, Berberisaristata, Ptychotisajowan, Cyperuspertenuis, Bombaxmalbaricum, Myristicafragrans, Panchamrutparpati, Aeglemarmelos	Tablet	Aravali Chemicals Private Limited
Kidney Formula	Gokshura, Punarnava, Guduchi, Manjista, Musta, Anantamul, Amalaki, Bibhitaki, Haritaki, Coriander, Fennel	Tablet	Banyan Botanicals
Jambril	Jambubij, SuddhaShilajit, Methi, Karela, GudmarButi, Mamejava, BilvaPatra, NeemPatra, AbharkBhasma, MuktaShuktiBhasma, KantlohBhasma,	Tablet	Unjha Pharmacy
Liver Formula	Bhumyamalaki, Guduchi, Kalmegh, Bhringraj, Punarnava, Manjista, Musta, Amalaki, Bibhitaki, Haritaki, Pippali	Tablet	Banyan Botanicals
Lung Formula	Licorice, Pippali, Vasaka, Amalaki, Bibhitaki, Haritaki, Tulsi, Cardamom, Cinnamon, Elecampane root	Tablet	Banyan Botanicals
Mental Clarity	Brahmi, Bacopa, Bhringaraj, Shankhapushpi, Ashwagandha, Vidarikanda, Pippali, Cardamom	Tablet	Banyan Botanicals
Triphala	Amalaki, Bibhitaki, Haritaki	Tablet	JivaAyurvedic Pharmacy Ltd.
Women's Cycle Nourish	Shatavari, Gokshura, Musta, Vidari, Kanda, Ashwagandha, Elecampane,	Tablet	Banyan Botanicals
Gasex	Chebulicmyrobalan, Bellericmyrobalan, Ginger, Black pepper, Indian gooseberry, Cowrie shell calx, Conch shell calx	Tablet	Himalaya herbal healthcare
Himplasia	Small caltrops, Bonduc nut, Asparagus Three leaved caper, Processed agate	Tablet	Himalaya herbal healthcare
Sudhasaptak Tablet	KapardiBhasma, GodantiBhasma, ShankhBhasma, MuktaShuktiBhasma,	Tablet	UnjhaAyurvedic Pharmacy
Pilex	Guggul, Shilajeet, Neem, Tree turmeric, Indian gooseberry, Chebulicmyrobalan, Beleric myrobalan, Indian laburnum, Kanchanara, Cobra's saffron	Tablet	Himalaya herbal healthcare
Digest tone	Amalaki, Bibhitaki, Haritaki, Cabbage rose	Tablet	Maharishi Ayurveda
Rumalaya Forte	Shallaki, Guggul, Java galangal, Licorice, Small caltrops,	Tablet	Himalaya herbal healthcare
Septilin	Indian bedellium, Conch shell calx, Gulanchatinospora, Indian madder, Indian gooseberry, Horse radish tree, Licorice	Tablet	Himalaya herbal healthcare

ODTs: Future aspects in context with herbal formulations

By applying different technique models the herbal formulations can be formulated so as to nullify the side effect caused by the comparative allopathic formulations.

Novel and unique quality control methods can be developed to determine the technological aspects of orally disintegrating tablets to define the characteristics of ODTs [25].

Applicability of ODT technology is there to a wide range of therapeutic agents including generics, thereby adding value, i.e. "supergenerics" for veterinary or human application [17-21]. Thus may be reliable for making the herbal formulations especially tablets.

Therapeutics basically based on protein and peptide used via oral route, have limited bioavailability when administered by immediate release tablets. Those kinds of products usually

degrade immediately in the GI system. By applying herbal ingredients complexing with high standard excipients in making such formulation may overcome on that, showing better results with no side effects. The developments of improved oral protein delivery Technology by oral dispersible tablets, that dispersed and/or dissolved in the saliva, are very promising for the delivery of high molecular weight protein and peptide [38].

It would be an innovative improvement in the ODT technology when development of ODTs using herbal ingredients with controlled release properties that can deliver drugs which has short half-lives like 12–24 hours. The added convenience and compliance of that kind formulations will be used more immensely [39].

The ability to formulate drugs in large doses will bring another important technological advance including herbal entity. Generally, the orally disintegrating tablet formulations require large amounts of excipients, and having large doses of drug will only make the final formulation too big to handle. ODT formulations that require fewer excipients with herbal ingredients including the drug itself will be a break through [41].

ODT technologies are in progress, but development of formulation of ODTs that contains lipophilic active pharmaceutical ingredients is a challenge whereas implementing the same for herbal formulation is even more challenging. New orally disintegrating tablet technology should be developed to find a solution for these problems [57]. From the literature survey it could be seen that there is not much delayed release ODTs in the market whereas not a single containing the herbal products. Controlled release orally disintegrating tablets and/or fixed dose combination of orally disintegrating tablet technologies can be developed as a next generation.

Conclusion

In conclusion, orally disintegrating tablets (ODTs) offer a novel approach for medication that has gained increasing importance in both the pharmaceutical industry and academia. ODTs offer several advantages over conventional tablets, including ease of administration, convenience, and increased bioavailability. However, the evaluation of ODTs presents some critical issues such as bioequivalence, stability, taste-masking, and manufacturing difficulties, which require innovative solutions. The use of herbal ingredients in ODTs also poses some unique challenges that require special attention. Despite these challenges, the future of ODTs looks promising with the potential for continued growth as new technologies and formulation techniques are developed. Overall, ODTs represent an essential alternative dosage form that can provide patients with a better therapeutic experience and improved outcomes.

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