TASTE MASKED ORODISPERSITE TABLETS: A HIGHLY PATIENT COMPLAINT DOSAGE FORM

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ABSTRACT

Objective: Table is still most popular conventional dosage forms existing today, but the drawback of solid dosage forms is the difficulty in swallowing (dysphagia) or chewing in some patients particularly pediatric and geriatric patients. For this reason, orodispersible tablets (ODT) that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. The main objective of this review is to explore various methodologies for masking the taste of obnoxious drugs, applications, evaluation and also the recent trends in taste masking technologies when prepare a ODT.

Methods: Pediatric and geriatric populations are the most sensitive to the bad taste of medicaments, thus in these cases patient compliance reduces. This reason is an initiative for the development of various taste masking technologies by which the characteristics of ODT is improved and good patient compliance is achieved.

Results: ODTs have better patient acceptance and compliance and may offer improved biopharmaceutical properties, improved efficacy, and better safety compared with conventional oral dosage forms. Prescription ODT products initially were developed to overcome the difficulty in swallowing conventional tablets among pediatric, geriatric, and psychiatric patients with dysphagia.

Conclusion: In this review, various techniques discussed which can help to overcome bitter taste of active pharmaceutical ingredients as well as largely improve the product preference among patients. It will also enhance the quality of the treatment provided to patients, especially children and older patients. Furthermore, various techniques could be combined to develop palatable and cost-effective ODTs.

Keywords: Orodispersible tablet, Taste masking, Patient compliance.

INTRODUCTION

The conventional dosage forms (tablet and capsule) have wide acceptance up to 50-60% of total dosage forms. The tablet is still most popular conventional dosage forms existing today because of ease of self-administration, compact in nature, easy to manufacture and it can be deliver inaccurate dose [1]. One important drawback of solid dosage forms is the difficulty in swallowing (dysphagia) or chewing in some patients particularly pediatric and geriatric patients. The problem of swallowing is a common phenomenon in geriatric patient due to fear of choking, hand tremors, dysphagia and in young individuals due to underdeveloped muscular and nervous systems and in schizophrenic patients which lead to poor patient compliance [2,3].

Difficulties in swallowing of tablet and capsule are also occurring when water is not available, in diarrhea, coughing during the common cold, allergy condition, and bronchial infection. Approximately one-third of the population (mainly pediatric and geriatric) has swallowing difficulties, resulting in poor compliance with oral tablet drug therapy which leads to reduced overall therapy effectiveness. For this reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention [4].

The United States Food and Drug Administration defined orodispersible tablet (ODT) as "a solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed on the tongue."

But in ODTs, taste is a crucial factor that determines the palatability of oral dosage form and patient compliance. It also gives a unique identity to a product. The oral route is considered the most convenient and easy route of drug delivery. Yet, patient noncompliance, termed “intelligent noncompliance,” due to feeling bitter, bad taste, etc., which is reasoned out by the patient but may not necessarily be wise, is one of the key causes of failure of oral dosage regimen [5]. Pediatric and geriatric populations are most sensitive to the bad taste of medicaments. Furthermore, currently, there is a rising trend to formulate drugs in the form of orally disintegrating dosage forms due to their easy ingestion and absorption process [6]. Thus, in these cases, a good taste is indispensable to patient compliance. Moreover, high palatability gives a competitive advantage, especially in the case of over the counter products [7,8].

NEED OF TASTE MASKED ODT

The fast dissolving solid dosage form turns into a soft paste or liquid form for easy swallowing, and thus, it is free of risk of choking and dissolves in saliva within a few seconds, and so-called true fast-dissolving tablets. Fast dissolving technology offers the following section [1,9].
• Improved compliance/addition convenience
• No water needed
• No chewing needed
• Better taste/have a pleasant mouth feel
• Improved stability
• Suitable for controlled as well as fast release actives
• Allows high drug loading
• Ability to provide advantages of liquid medication in the form of solid preparation
• Adaptable and amenable to existing processing and packaging machinery
• Cost-effective.

CHARACTERISTIC OF TASTE MASKED ODT

This novel dosage form, have several characteristics to distinguish them from the more traditional dosage forms. Traditional tablet formulations generally do not require taste masking, because it is assumed that the dosage form will not dissolve until passing the oral cavity. Many oral suspensions, syrups, and chewable tablets simply contain flavors, sugars, and other sweeteners to overcome the bitter taste of the drug.
In fast-dissolving/disintegrating tablets include sweeteners and flavors for taste-masking, but many drugs are extremely bitter and that bitter taste cannot be masked by taste masking agent. In these cases, taste is masked by various technologies as given below then they are converted into FDT. Some other characteristics are as follows [1,7]:

- The taste masked ODT should not leave an unpleasant taste into the oral cavity.
- It should disintegrate within the 15 seconds to 3 minutes without need of water.
- It should have sufficient mechanical strength.
- The particle size of drug candidate should be fine so that it provides better surface area for the absorption to enhance bioavailability.
- Drug candidate should be absorbed throughout the GIT.
- It should have good solubility for dissolution.

**POLYMER AND TECHNIQUES USED FOR TASTE MASKING**

- An appropriate taste masking technique can affect both product quality and process effectiveness. Following are various taste masking techniques along with their polymer that can be used to taste mask bitter active pharmaceutical ingredient.
  - Sweetener, flavorant, and other excipient addition
  - Complexation
  - Coating
  - Ion exchange resins
  - Matrix entrapment
  - Prodrug formation
  - Salt formation
  - Miscellaneous.

**Sweetener, flavorant, and other excipient addition**

This is one of the simplest techniques used in taste masking. Excipients such as sweeteners and flavorants can be added to taste mask bitter active pharmaceutical ingredients (API)/drug. Sweeteners, being highly water soluble, dissolve in saliva and coat the taste buds, thereby retarding the interaction of bitter API with taste buds. Flavorants enhance the formulation and give it a distinct taste. They are to be added in addition to primary taste masking agent. Certain cooling flavorants such as menthol numb the taste buds and retard bitter taste perception. In addition, other excipients such as bitterness inhibitors can also be added. Some examples of sweeteners and flavorants [1,10], i.e., aspartame, acesulfame potassium, cyclamate, glycyrrhizin, lactose, mannitol, saccharin, sucrose, and sucralose (Table 1).

**Complexation**

In complexation, the drug molecule fits into the cavity of a complexing agent, i.e., the host molecule, forming a stable complex. Complexation decreases the amount of drug particles, which are exposed to taste buds, thereby reducing the perception of bitter taste. Inclusion complex is a “host-guest” relationship in which the host is complexing agent and guest is the active moiety. The complexing agent is capable of masking bitter taste either by decreasing its oral solubility or decreasing the availability of drug to taste buds. Vander Waal forces are mainly involved in inclusion complexes. β-cyclodextrin is widely used complexing for taste masking of drugs due to its sweet taste and is nontoxic in nature [1,11], e.g., anethol-β-cyclodextrin complex and saccharin, hydroxypropyl β-cyclodextrin, β-cyclodextrin, γ-cyclodextrin, and tannic acid.

**Coating**

The coating is one of the best methods of taste masking. It can involve coating of a tablet containing bitter API or coating of the bitter API particles themselves. Ideally, the polymers selected in coating should be such that they prevent API release in oral cavity and allow its release in the absorption window of the API. The coating material is classified into lipids, polymers, and sugars. These materials can either be used alone or in combinations, as a single layer or multiple layer coats to achieve taste masking of the bitter drugs. Hydrophobic polymers have been popularly used for coating of bitter drugs than hydrophilic polymers to achieve taste masking. Sweeteners can also be incorporated in the coating solution of better taste masking [1,12] (Table 2).

Microencapsulation is a process in which the active moiety (solid or liquid droplets) is coated with a polymeric material or film. Types of microencapsulation include air suspension coating, coacervation phase separation, spray drying, spray congealing, solvent evaporation, pan coating, and interfacial polymerization. Of these processes, first four are mostly used techniques for achieving taste masking.

**Ion exchange resins**

Ion exchange resins are synthetic organic polymers inert in nature, consists of a hydrocarbon chain to which insoluble groups are attached, and they have ability to exchange their labile ions for ions present in the solution with which they are in contact.

Based on the charge of the functional groups present, ion exchange resins are classified into cation exchange resins and anion exchange resins. Within each category, they are classified into strong and weak depending on their affinity for counter ions. Cation exchange resins are exchangers of sodium, potassium or aluminum salts, and anionic resins are for chloride ions. The drugs are loaded onto the resins by column method and batch method [9] (Table 3).

**Matrix entrapment**

Matrix entrapment involves trapping of drug into bulky matrix and thereby retarding its contact with taste buds. The matrix may contain polymeric, resinous, gelling, or liposomal materials [9,13].

**Prodrug formation**

Prodrugs are molecules that are initially inactive but, upon biotransformation, are converted to active forms. Prodrug formation leads to physicochemical modification of bitter loci and thereby inhibits/retards their interaction with taste receptors. Other advantages of prodrugs include change in aqueous solubility, increase lipophilicity, improved absorption, less side effects, and change in membrane permeability [14].

**Salt formation**

Salt formation usually retards the solubility of API in saliva and thereby retards its taste perception [1,15].

*Table 1: Selection of flavors based on sensation of taste*

<table>
<thead>
<tr>
<th>Sensation</th>
<th>Flavor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salt</td>
<td>Butterscotch, apple, apricot, peach, vanilla</td>
</tr>
<tr>
<td>Bitter</td>
<td>Wild cherry, walnut, chocolate, mint, passion fruit</td>
</tr>
<tr>
<td>Sweet</td>
<td>Fruit and berry, vanilla</td>
</tr>
<tr>
<td>Sour</td>
<td>Citrus flavors, liquorice, not beat, raspberry</td>
</tr>
</tbody>
</table>

*Table 2: List of different types of polymers with examples*

<table>
<thead>
<tr>
<th>Type of polymer</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water soluble</td>
<td>Cellulose acetate butyrate, PVP</td>
</tr>
<tr>
<td>Water insoluble</td>
<td>hydroxyl ethyl cellulose</td>
</tr>
<tr>
<td>polymers</td>
<td>Ethyl cellulose, polyvinyl acetate</td>
</tr>
<tr>
<td>pH dependent Water insoluble polymers</td>
<td>crosspovidone, crosscaramellose</td>
</tr>
<tr>
<td>pH dependent Water</td>
<td>Polycarbofull, polyacrylic acid</td>
</tr>
<tr>
<td>Insoluble polymers</td>
<td>Cellulose ethers, cellulose ester, polyvinyl acetate</td>
</tr>
<tr>
<td>Reverse enteric polymers</td>
<td>Eudragit E 100, Eudragit EPO, methyl methacrylate, hydroxyl ethyl methacrylate, vinyl</td>
</tr>
<tr>
<td>Enteric polymers</td>
<td>Pyridine, Pthalate, hydroxyl pthalates, acrylic acid esters</td>
</tr>
<tr>
<td>Spacing layer polymers</td>
<td>Ethyl cellulose: PVP</td>
</tr>
</tbody>
</table>

PVP: Polyvinyl pyrrolidone
Amberlite IR 120, Polystyrene-DVB
Amberlite IR 4B, Polystyrene-DVB
Amberlite IRP, Polystyrene-DVB
Methacrylic acid-DVB

Singh and Verma

Recent developments in the field of taste masking

Stimuli-responsive drug delivery systems incorporating pH sensitive, ion-sensitive polymers have been developed for masking bitter API taste [22]. Lycopodium derived microcapsules have been used to taste mask ibuprofen [23]. Techniques, such as nano hybridizing and wet spherical agglomeration, have also been used for taste masking [24,25].

TECHNIQUES USED FOR PREPARATION OF ODT

- Freeze drying/lyophilization
- Spray drying
- Molding
- Sublimation
- Mass extrusion
- Direct compression
- Phase transition process
- Cotton Candy Process
- Nanization.

Freeze drying/lyophilization
Lyophilization means drying at low temperature under condition that involves the removal of water by sublimation. Drug in a water soluble matrix which is then freeze-dried to give highly porous structure. The tablets prepared by lyophilization disintegrate rapidly in <5 seconds due to quick penetration of saliva in pores when placed in the oral cavity. Lyophilization is useful for heat sensitive drugs, i.e., thermolabile substances [26,27].

Spray drying
This technique is based on a particulate support matrix, which is prepared by spray drying an aqueous composition containing support matrix and other components to form a highly porous and fine powder. This then mixed with active ingredients and compressed into tablets. The formulations are incorporated by hydrolyzed and non-hydrolyzed gelatins as supporting agents, mannitol as bulking agent, sodium starch glycolate or croscarmellose sodium as disintegrating and an acidic material (e.g., citric acid) and/or alcali material (e.g., sodium bicarbonate) to enhance disintegration and dissolution. Tablet compressed from the spray dried powder disintegrated within 20 seconds when immersed in an aqueous medium [28].

Molding
Tablets prepared by this method are solid dispersions. Molded tablets offer improved taste due to water soluble sugars present in dispersion matrix. The molding process is of two types, i.e., solvent method and heat method. The solvent method involves moistening the powder blend with a hydroalcoholic solvent followed by compression at low pressures in molded plates to form a wetted mass (compression molding). The solvent is then removed by air-drying. The tablets manufactured in this manner are less compact than compressed tablets and possess a porous structure that hastens dissolution. The heat molding process involves preparation of a suspension that contains a drug, agar and sugar (e.g., mannitol or lactose) and pouring the suspension in the blister packaging wells, solidifying the agar at the room temperature to form a jelly and drying at 30°C under vacuum [29].

Sublimation
In this method, a subliming material (such as ammonium bicarbonate, ammonium carbonate, urea, benzoic acid, naphthalene, and camphor) is removed by sublimation from compressed tablets and high porosity is achieved due to the formation of many pores, where camphor particles previously existed in the compressed tablets prior to sublimation of the camphor. A high porosity was achieved due to the formation of many pores, where camphor particles previously existed in the compressed tablets prior to sublimation of the camphor. These compressed tablets which have high porosity (approximately 30%) rapidly dissolved within 15 seconds in saliva [30].

Mass extrusion
This technology involves softening of the active blend using the solvent mixture of water soluble polyethylene glycol and methanol and expulsion of softened mass through the extruder or syringe to get a cylindrical shaped extrude which are finally cut into even segments.
using heated blade to form tablets. This process can also be used to coat granules of bitter drugs to mask their taste [31,32].

**Direct compression**
Direct compression represents the simplest and most cost-effective tablet manufacturing technique. The addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipients and effervescent agents further hastens the process of disintegration [33].

**Phase transition process**
FDTs were produced by compressing powder containing erythritol (melting point: 122°C) and xylitol (melting point: 93-95°C), and then heating at about 93°C for 15 minutes. After heating, the median pore size of the tablets was increased and tablet hardness was also increased. The increase of tablet hardness with heating and storage did not depend on the crystal state of the lower melting point sugar alcohol [34].

**Cotton candy process**
This process utilizes a unique spinning mechanism to produce floss-like crystalline structure. Cotton candy process involves the formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to improve flow property and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to orally disintegrating tablet. This process can accommodate larger drug doses and offers improved mechanical strength. However, high process temperature limits the use of this process [32,34].

**Nanomization**
A recently developed nanomelt technology involves reduction in the particle size of drug to nanosize by milling the drug using a proprietary wet-milling technique [34]. The nanocrystals of the drug are stabilized against agglomeration by surface adsorption on selected stabilizers, which are then incorporated into mouth dissolving tablets. This technique is especially advantageous for poor water soluble drugs. Other advantages of this technology include fast disintegration/dissolution of nanoparticles leading to increased absorption and hence higher bioavailability and reduction in dose, cost-effective manufacturing process, conventional packaging due to exceptional durability and wide range of doses [31].

**IMPORTANT PATENTED TECHNOLOGIES IN ODTs**

**Zydus**
This drug delivery system consists of freeze-dried tablets having active drug designed to rapidly disintegrate in the mouth. The freeze-dried tablet is made by lyophilizing a suspension or solution of drug containing various excipients such as polymer, polysaccharides, preservatives, pH adjusters, flavors, sweeteners, and colors, which is then filled in blisters. Freeze drying occurs in the blisters, which are then sealed and further packaged. Some of the advantages of the zydus system include fast disintegration time. Some of the disadvantages include low throughput, high cost of goods, and limited taste masking [35].

**OraSolv, DuraSolv, and PakSolv**
The ingredients contained in the technology include polyols as fillers, disintegrant, which may include an effervescence couple, flavor, sweetener, and lubricant. The drug may be taste masked if required typically utilizing a fluid bed coating process. The tableting process includes direct compression, and can accommodate a wide range of potency from <1 mg to as high as 500 mg. Tablets manufactured with OraSolv technology should contain an effervescence couple along with microparticles of drug within a rupturable coat. The tablets manufactured are compressed at a low hardness that promotes fast disintegration. The dosage forms need to be packaged in aluminum foil blisters with a dome shape that impacts physical protection and impermeability to moisture [36].

**Lyoc**
This was the first freeze drying based technology introduced for ODTs. The process involves preparation of a liquid solution or suspension of the drug containing fillers, thickening agents, surfactants, non-volatile flavoring agents, and sweeteners. This homogenous liquid is then deposited in blister cavities and subjected to freeze drying [37].

**Flashtab**
Flashtab tablet matrix consists of a swellable agent (modified starch or microcrystalline cellulose) and a super disintegrant (crosprimed or crosscarmellose). The system may also contain, depending on the need, a highly water-soluble polyol with binding properties such as mannitol, sorbitol, maltitol, or xylitol, instead of the swellable agent as mentioned before. The active is taste masked by direct coating. Tablets manufactured using this technology produce durable tablets in which the excipients are first granulated using wet or dry granulation process, then the coated drug is mixed with the excipient granules and compressed into tablets that can be handled and packaged using conventional processing equipment. Tablets for blister packaging can withstand the pressure used to push the tablet out of the lidding foil of the blister card. Tablets containing hygroscopic material can also be blister packaged, using high-quality polyvinyl chloride or aluminum foils, which provide a higher degree of moisture protection than ordinary polyvinyl chloride or polypropylene foils [38].

**Flash dose**
FlashDose tablets containing a matrix of these sugar fibers disintegrate very rapidly on contact with saliva, with disintegration times of a few seconds. The tablets produced by FlashDose are hydrophilic and highly porous, owing to relatively low compression during the pressing of the tablets. For taste masking, Fuisz uses its own patented, single-step, solvent-free process, termed “CEFORMTM technology,” which produces uniform microspheres with a very narrow particle size distribution. The resulting tablets produced by this process are soft, friable, and highly moisture sensitive. They require specialized packaging materials and processes to protect them from external humidity and mechanical abrasion [39].

**Wow tab**
Wow tab technology is patented by Yamanouchi Pharmaceutical Co. In this process, a combination of low mold ability saccharides with hardness 0-2 kg and high moldability saccharides with hardness more than 2 kg is used to obtain a rapidly melting strong tablet. The active ingredient is mixed with a low moldability saccharide, e.g., lactose, glucose, and mannitol and granulated with a high mold ability saccharide, e.g., Maltose, Oligosaccharides and compressed into tablet [40].

**Pharmaburst technology**
Pharmaburst is a co-processed excipient system which involves a dry blend of a drug, flavors, and lubricant then followed by compression into tablets which then dissolve within 30-40 seconds. Tablets manufactured by this methodology have sufficient strength can be packed in blister packs and bottles [41].

**FrostaTM**
The technology incorporates manufacture of highly plastic granules using a plastic material, a material enhancing water penetration, and a wet binder. These granules can then be compressed into tablets at low pressure, thus enabling fast disintegration on administration. The tablets obtained have excellent hardness and rapid disintegration time ranging from 15 to 30 seconds depending on size of tablet [42].

**Quicksoolv technology**
In the Quicksoolv formulation, the matrix compositions are dissolved in the solvent (usually water), and then this solution is frozen. At the temperature, the first solvent will remain in the solid form, and then the frozen solution contacts the second solvent which is usually, ethanol,
menthol, or acetone. Thus, the first solvent is removed after a few hours of contacting the second solvent to result in a usable matrix. The final product disintegrates almost instantly. This method is claimed to prevent or to reduce the incidence of cracking during the final preparation, having uniform porosity and also the adequate strength for handling [43].

**Nanocrystal technology**

Nanocrystal technology includes lyophilization of colloidal dispersions of drug substance and water-soluble ingredients filled into blister pockets. This method avoids manufacturing process such as granulation, blending, and tableting, which is more advantageous for highly potent and hazardous drugs. As manufacturing losses are negligible, this process is useful for small quantities of drug [44].

**Ziplets advatab**

It utilizes water-insoluble ingredient combined with one or more effective disintegrants to produce ODT with improved mechanical strength and optimal disintegration time at low compression force. This technology handles high drug loading and coated drug particles and does not require special packaging, so they can be packed in push through blisters or bottles [45].

**EVALUATION OF ODTs**

**Tablet thickness**

Tablet thickness is an important characteristic in reproducing appearance and also in counting using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Thickness was recorded using Vernier Calliper [46].

**Weight variation**

About 20 tablets were selected randomly from the lot and weighted individually to check for weight variation as per I.P.

**Friability**

Friability attempts for decreasing the disintegration time increase the friability of ODTs than the conventional tablets. Dosage forms like Zydus are very fragile. Friability is a measure of mechanical strength of the tablet. If a tablet has more friability it may not remain intact during packaging, transport or handling. Roche friabilator is used to determine the friability by following procedure. Pre-weighed tablets are placed in the friabilator. Friabilator consists of a plastic chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets are rotated in the friabilator for at least

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**Table 4: Ideal candidates for taste masked ODTs**

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Contribution</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>1997</td>
<td>Koizumi</td>
<td>New method of preparing high porosity rapidly saliva soluble compressed tablets using mannitol with camphor, a subliming material.</td>
<td>[30]</td>
</tr>
<tr>
<td>2008</td>
<td>Shah and Sharma</td>
<td>Development and evaluation of artemether taste masked rapid disintegrating tablets with improved dissolution using solid dispersion technique</td>
<td>[1]</td>
</tr>
<tr>
<td>2009</td>
<td>Kumar et al.</td>
<td>Development and characterization of mel-in tablets of Haloperidol by sublimation technique</td>
<td>[31]</td>
</tr>
<tr>
<td>2009</td>
<td>Malke et al.</td>
<td>Novel melt granulation using sugars for metoclopramide hydrochloride orally disintegrating tablet</td>
<td>[50]</td>
</tr>
<tr>
<td>2010</td>
<td>Torne et al.</td>
<td>Fast disintegrating tablets of ondansetron hydrochloride by direct compression technique</td>
<td>[51]</td>
</tr>
<tr>
<td>2010</td>
<td>Dahima and Sharma</td>
<td>Formulation and in vitro evaluation of taste masked ODT of metoclopramide hydrochloride using indion 204</td>
<td>[52]</td>
</tr>
<tr>
<td>2010</td>
<td>Pandey et al.</td>
<td>Formulation and evaluation of taste masked fast disintegrating tablets of lisinopril</td>
<td>[53]</td>
</tr>
<tr>
<td>2010</td>
<td>Puttewar et al.</td>
<td>Formulation and evaluation of ODT of taste masked doxylamine succinate using ion exchange resin</td>
<td>[54]</td>
</tr>
<tr>
<td>2011</td>
<td>Masareddy et al.</td>
<td>Development of orodispersible tizanidine HCl tablets using spray dried coprocessed excipient bases</td>
<td>[29]</td>
</tr>
<tr>
<td>2012</td>
<td>Remya et al.</td>
<td>Formulation and evaluation of fast disintegrating ODTs of ondansetron hydrochloride</td>
<td>[56]</td>
</tr>
<tr>
<td>2013</td>
<td>Thakare et al.</td>
<td>Development of metoclopramide hydrochloride orodispersible tablets using taste masking tulson 339</td>
<td>[57]</td>
</tr>
<tr>
<td>2014</td>
<td>Deshmukh et al.</td>
<td>Lyophilized with dry silica</td>
<td>[58]</td>
</tr>
<tr>
<td>2014</td>
<td>Gupta et al.</td>
<td>Fast disintegrating combination tablet of taste masked levo cetirizine dihydrochloride and montelukast sodium: Formulation design, development, and characterization</td>
<td>[59]</td>
</tr>
<tr>
<td>2015</td>
<td>Alshehri et al.</td>
<td>Mefenamic acid taste-masked oral disintegrating tablets with enhanced solubility via molecular interaction produced by hot melt extrusion technology</td>
<td>[8]</td>
</tr>
<tr>
<td>2015</td>
<td>Tripathi and Mayle</td>
<td>Formulation and evaluation of taste masked ODT of levo cetirizine dihydrochloride</td>
<td>[60]</td>
</tr>
</tbody>
</table>

ODT: Orodispersible tablets
4 minutes [46]. At the end of test, tablets are dusted and reweighed; the loss in the weight of tablet is the measure of friability and is expressed in percentage as:

\[
\% \text{Friability}=1-(\text{loss in weight/Initial weight})\times100
\]

**Hardness (crushing strength)**

Tablet hardness is measured with hardness testers like Monsanto. A tablet is placed in the hardness tester and load required to crush the tablet is measured. The hardness of ODTs is generally kept lower than conventional tablets as increased hardness delays the disintegration of the tablet. The force is measured in kg and the hardness of about 3-5 kg/cm² is considered to be satisfactory for uncoated tablets [46].

**Water absorption ratio**

A small piece of tissue paper folded twice is placed in a small petridish containing 6 ml of water. Put a tablet on the paper and the time required for complete wetting is measured [46]. The wetted tablet is then reweighed. Water absorption ratio, R is determined by using following formula:

\[
R=100\times\frac{W_s-W_t}{W_s}
\]

Where, \(W_s\) is the weight of tablet before water absorption and \(W_t\) is the weight of tablet after water absorption.

**Uniformity of dispersion**

Keep the two tablets in 100 ml water and stir gently for 2 minutes. The dispersion is passed through 22 meshes. The tablets will consider passing the test if no residue remained on the screen.

**Disintegration time**

According to the European pharmacopoeia the fast disintegrating or ODTs should disintegrate within 3 minutes without leaving any residue on the screen. However, it is difficult to assess the disintegration rate even in small amounts of water. Further the conventional test employs a volume of 900 ml of distilled water compared to the volume of saliva in humans, which is limited to a few ml. Thus, the disintegration rate obtained from conventional test does not appear to reflect the actual disintegration rate in human mouth. To overcome these problems, several new methods have been proposed [46].

**In vivo disintegration time**

In vivo disintegration time is determined using a panel of healthy human volunteers. The disintegrating time noted by the volunteers by placing the tablet in mouth [46].

**Dissolution test**

The dissolution method for oral disintegrating tablets is the same as that of conventional tablets. USP 2 paddle apparatus is most suitable and common choice for dissolution test of oral disintegrating tablets, where the paddle speed is 50 rpm is used. The USP 1 (basket) apparatus may have certain application for such tablets but is used less frequently due to specific physical properties of tablets [46].

**IN VITRO CHARACTERIZATION OF TASTE MASKED ODT**

**In vitro methods**

In vitro methods such as spectrophotometry involve mixing of formulation to 10ml distilled water and then analyzing API concentration. If API concentration is below the threshold, sufficient taste masking is considered to be achieved.

The spectrophotometry method is not an absolute taste evaluation test. Another in vitro test involves usage of the electronic (e) tongue to evaluate taste. The e-tongue emulates the three levels of biological taste recognition: The receptor level (taste buds in humans, probe membranes in the e-tongue), the circuit level (neural transmission in humans, transducer in the e-tongue), and the perceptual level (cognition in the thalamus in humans, computer and statistical analysis in the e-tongue). In e-tongue, the formulation or API is evaluated against standard (e.g., quinine hydrochloride) and the software generates taste patterns that form the basis of evaluation [15,47].

**IN VIVO CHARACTERIZATION OF TASTE MASKED ODT**

**In vivo tests**

In vivo tests such as human panel testing and frog taste nerve responses can be used to evaluate taste of formulations. In human panel testing, large groups of healthy volunteers are asked to take bitter drug and then the taste-masked formulation. They are then asked to comparatively rate the formulation on various organoleptic properties. In frog taste nerve responses, glossopharyngeal nerve of bullfrogs is connected to AC amplifier and responses to bitter drug and formulation are taken. The peak height obtained is used to assess taste masking [48,49] (Table 4).

**CONCLUSION**

ODTs have better patient acceptance and compliance and may offer improved biopharmaceutical properties, improved efficacy, and better safety compared with conventional oral dosage forms. Prescription ODT products initially were developed to overcome the difficulty in swallowing conventional tablets among pediatric, geriatric, and psychiatric patients with dysphagia. In this review, various techniques discussed which can help to overcome bitter taste of API as well as largely improve the product preference among patients. It will also enhance the quality of the treatment provided to patients, especially children and older patients. Furthermore, various techniques could be combined to develop palatable and cost-effective ODTs.

**REFERENCES**

