REVIEW

NEW TECHNOLOGIES IN THE FORMULATION OF ORAL DISPERSIBLE TABLETS AND TASTE MASKING: A REVIEW

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ABSTRACT:
In oral drug delivery system (ODDS), drug is administered through the oral route. Oral route is the most preferred and safe route for the delivery of dosage form. Enzymatic degradation of drug and first pass metabolism are the main drawback for this route. One of the tablet taken through this route is Oral dispersible tablet (ODT) is also known as Fast melting, Fast-dispersing, Fast dissolving, Mouth dissolving and Quick disintegrating tablet. These are the tablets which are intended to be placed in the mouth where before swallowing they are get to disperse rapidly. These tablets are made for the fast action basically due to their fast dispersion. ODTs having many merits such as water is not required for swallowing these tablets, having no difficulties for administration to geriatric, paediatric, mentally disabled, and bed-ridden patients these are having rapid onset of therapeutic action, give good mouth feels, particularly for paediatric patients. Some techniques to prepare ODT are Freeze-drying (Lyophilisation), spray drying, melt granulation, cotton candy process, Phase transition process and direct compression etc. But for these tablets the main challenge is the taste of drug. If the drug having bitter taste it becomes very difficult to take the tablet in this dosage form. However there are many taste masking techniques have been come in focus today to solve this problem. Some of taste masking techniques are such as flavouring and sweetening agents addition, Ion exchange resin, Adsorption, Granulation, Microencapsulation, Prodrug approach, Bitterness inhibitor, Solid dispersion system, Gel formation etc.

KEYWORDS: Oral drug delivery system (ODDS), Oral dispersible tablet (ODT), Gastrointestinal tract (GIT), Direct compressible (DC).

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INTRODUCTION

Oral drug delivery system (ODDS)

The oral route is the most important, safest and convenient method of administration of the drug. Oral drug delivery system generally includes substances to mask the taste of the active ingredients and in the pharmaceutical industries, it is considered as gold standard. This masked active ingredient is then swallowed by the patient's saliva along with the soluble and insoluble excipients. More than 70% of drugs are available on the market in the form of oral drug delivery. The various routes of drug delivery, the oral route is perhaps the most preferred by patients and clinicians. Oral route has disadvantages when drugs in tablet form are administered through this route. Disadvantages are such as enzymatic degradation within the gastrointestinal tract (GIT) and hepatic first-pass metabolism, due to prohibition of oral administration of certain classes of drugs i.e. peptides and proteins. The phenomenon of drug absorption where before the drug reaches the systemic circulation the concentration of it prominently reduced is known as first-pass metabolism or systemic metabolism. Trans mucosal routes of drug delivery offer distinct advantages over peroral administration for systemic effect such as a possible bypass of first pass effects and avoidance of systemic elimination within the GI tract. Although they offer advantages because of poor patient acceptability associated with this site, they are preferred for the local application rather than systemic application. The oral cavity is highly acceptable by patients.[1-3]

Most of the chemical entities are lipophilic in nature and these entities can be administered through the oral route. The oral cavity is highly preferred as a route of administration as the mucosa is permeable with a rich blood supply.[4,5]

Oral Mucosa

The oral cavity is the main site for entry of food and air into the body where as mouth and lips are also essential to human for speech, by modifying the passage of air. The oral cavity is confined between dental arches on the teeth which are occupied by the tongue large muscles attached to the floor of the mouth by the frenulum langue[6,7]

1.1.2 Absorption of drug during oral mucosa:

The buccal mucosa is about 500-800 µm thick. The gingival mucosa which includes hard and soft palate, the floor of the mouth, ventral tongue and the gingiva is about 100-200 µm thick. The turnover time is 3-8 days and 14-18 days respectively. The salivary glands are shown in figure 1.

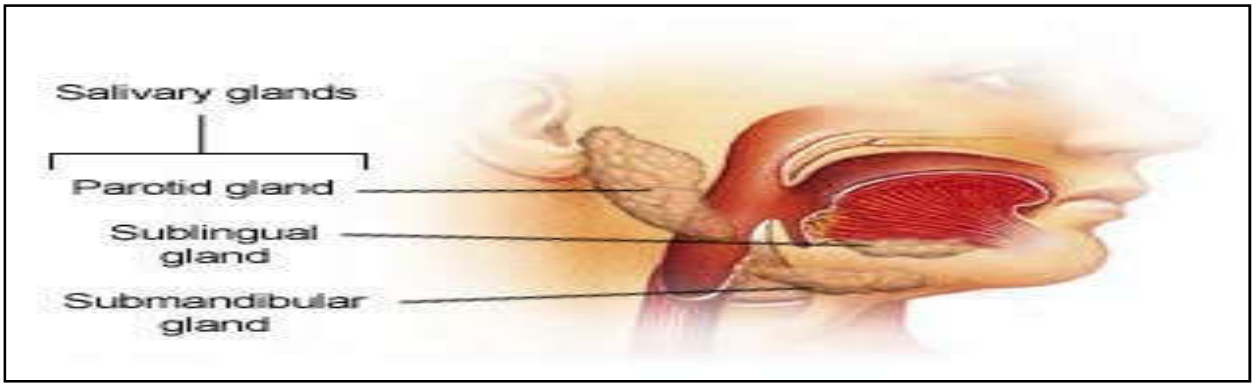

Figure 1: Types of salivary glands

Saliva plays an important role with a pH around 5.5-7.5, depending upon the stimulation of salivary glands. The thickness of salivary films is around 10-100 µm and normally human produce saliva at a rate of 1 liter/day, the resting flow is 0.5 ml/min and it increases up to 7 ml/min[6,7]. The oral cavity is rich in blood vessels and lymphatic, so a rapid onset of action and high blood levels of drugs are obtained quickly. In order to absorb orally, the drug must be dissolved in the saliva. Extremely hydrophobic materials will not dissolve well and are likely to be swallowed intact unless a specialized delivery system is used to prevent them to the mucosa[6].

Oral dispersible tablet

Oro-dispersible tablet is also known as "*Fast melting, Fast-dispersing, Fast dissolving, Rapid dissolve, Rapid melt, Mouth dissolving* and *Quick disintegrating tablet"*.

European Pharmacopoeia describes ODTs as "*Uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed and as tablets which should disintegrate within 3 min"*. FDA defines ODT as "*A solid dosage form which contains a medicinal substance or active ingredient which disintegrates rapidly within a matter of seconds when placed upon a tongue*". The significance of these dosage forms is highlighted by the adoption of the term, "*Oro-dispersible tablet*", by the European Pharmacopoeia (EP) which describes it "*as a tablet that can be placed in oral cavity where it disperses rapidly before swallowing"*[8,9].

A new generation formulations provide the simplicity of a tablet formulation and also allow the simplicity of swallowing provided by a liquid formulation and having many significances for liquid and conventional tablet formulations, are oral dispersible tablets[2]. In contact with saliva, these dosage forms fastly disintegrate and dissolve. The faster the drug into solution, quicker the absorption , and the onset of clinical effects[9]. Some drugs are absorbed from the mouth, pharynx, and oesophagus as the saliva passes down into the stomach[10]. If solid dosage forms turn into a soft paste or liquid form for easy swallowing, and thus it is free of risk of choking that's why mouth dissolving tablets are designed, it rapidly disintegrates and no need of water[11].

Indications for Oral dispersible tablets

Dysphagia

It is estimated that approximately 50% of the general population have difficulties in swallowing tablets and capsules. Difficulty in swallowing is known as dysphagia.

Presbysphagia is age-related functional changes in swallowing process. When the swallowing functions are affected beyond the normal aging by pathological conditions, as co-morbidities or by drug therapies, the swallowing disorder is referred to as ***Dysphagia.***[12]

Some pathological conditions are enlisted in Table 1

Table 1: Pathological conditions causing Dysphagia[12]

Central nervous	Musculoskeletal	Metabolic
Stroke	Polyneuropathy	Myasthenia gravis
Alzheimer's disease	Down's syndrome	Zenker diverticulum
Parkinson's disease	Spinal muscular atrophy	Diabetes
Dementia syndrome	Oculo pharyngeal dystrophy	Hyper and hypotension
Motor neuron disease		
Multiple sclerosis		
Schizophrenia		

Thus the problem of dysphagia caused by all factor mentioned above can overcome by the oral dispersible tablet.[8,12,13]

Persistent vomiting

The anti-emetic drugs are often administered to prevent nausea and vomiting associated with radiation therapy, after operative procedures, during pregnancy, and in the treatment of gastrointestinal tumors. Persistent vomiting results in loss of hydrochloric acid, alkalosis, and dehydration, which in turn may precipitate further vomiting. Hence, when this condition prevails the patient cannot swallow even a small quantity of fluid. Thus, swallowing conventional tablet with water is not possible. Hence, ODT seems to offer the distinct advantage over its conventional tablet form in terms of ease of administration and enhance pre-gastric absorption, thereby ensuring immediate effect.[13-15]

Other Patient factors:

- Patients who are unwilling to take solid preparation due to fear of choking.

- A patient having little access to water.
- Mentally retarded and uncooperative patients prefer ODTs.
- A middle-aged woman undergoing radiation therapy for breast cancer may be too nauseous to swallow H_2-blocker.

Ideal properties of ODTs[10,11,16]

The action of ODTs depends on upon the manufacturing technology and having the capability of fast disintegrating or dissolving in the saliva without the need of water. ODTs have found some ideal individuality to differentiate them from traditional conventional dosage forms. Important significance of these dosage forms includes:

- It is convenient and easy to administer.
- High drug loading is also allowed.
- It gives agreeable feeling in the mouth.
- It is also companionable with taste masking and other excipients.
- In oral administration, it leaves negligible or no residue in the mouth.
- It also has sufficient strength to withstand the rigors of the manufacturing process and post-manufacturing handling.
- It is insensitive to environmental conditions such as humidity and temperature.

Merits of ODTs[17,18]

- Having no difficulties for administration to geriatric, pediatric, mentally disabled, and bed-ridden patients.
- Water is not required for swallowing.
- Having rapid onset of therapeutic action.
- Good mouth feels, particularly for pediatric patients.
- Due to physical obstruction having minimum risk of suffocation in airways. Rapid drug therapy intervention is possible.
- At low-cost conventional processing and packaging, equipment allow the manufacturing of tablets.

Techniques for ODT formulation[8,9]

Many techniques have been reported for the formulation of ODTs. Which are enlisted in Table 2.

Table 2: Various techniques to produce ODTs[8,9]

Various Techniques to produce ODTs

1. Freeze-drying (Lyophilization).	**7. Melt granulation.**
2. Tablet molding.	**8. Phase transition process.**
3. Spray-drying.	**9. Cotton candy process.**
4. Direct compression.	**10. Nanonization.**
5. Sublimation.	**11. Fast dissolving films.**
6. Mass extrusion.	

1. Freeze Drying (Lyophilization)[19,20]

Freeze drying (Lyophilization) is a process in which water is sublimed from the product after it is frozen. This technique creates an amorphous porous structure that can dissolve rapidly. The big demerit of this technique is expensive and time-consuming. Various steps involved in freez drying are shown in figure 2.

Advantages:

- Highly porous product.
- Have high specific surface area.
- Improved absorption and bioavailability.

Disadvantages:

- It is time-consuming manufacturing process and expensive.
- At higher temperature and humidity it shows poor stability.

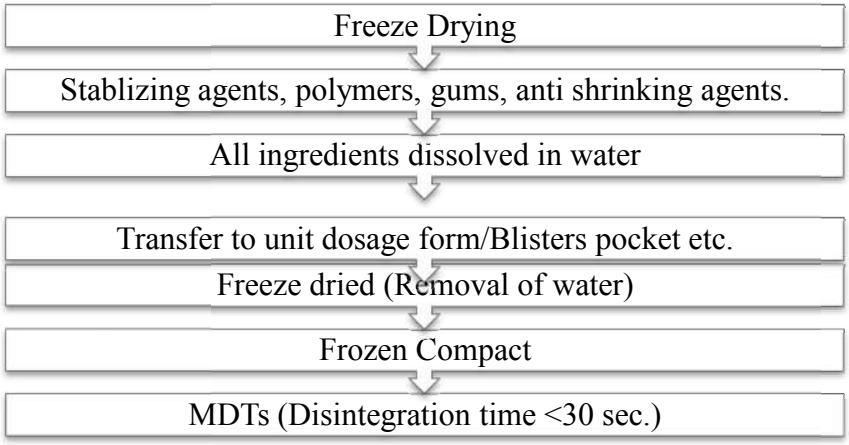

Figure 2: Steps involved in Freez Dring[19,20]

2. Tablet Moulding[9]

It is of two types-

a. Solvent method
b. Heat method

a. Solvent method[19]

This method involves moistening the powder blend with a hydro-alcoholic solvent followed by compression at low pressures in molded plates to form a wetted mass. By using air-drying method the solvent is then removed.

b. Heat method[21]

In this process suspension is prepared which contains a drug, agar and sugar (e.g. mannitol or lactose) and then this suspension is poured in the blister packaging walls followed by solidifying the agar to form a jelly at the room temperature and drying at 30°Cunder vacuum. But an additional problem to this technology is taste masking. Various steps involved in tablet molding are shown in figure 3.

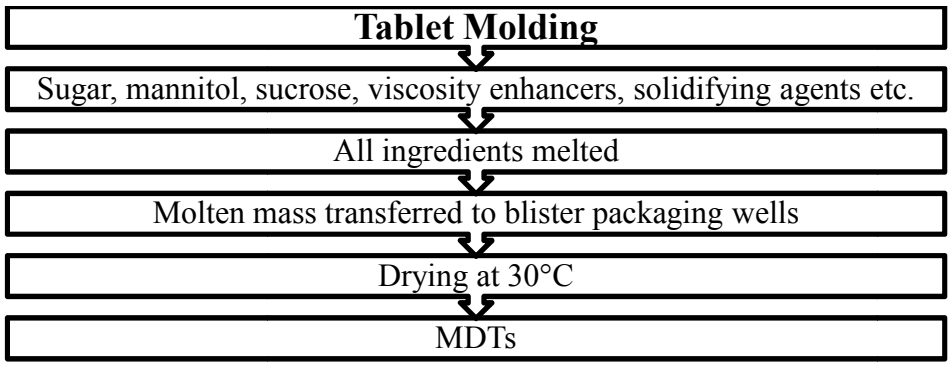

Figure 3: Steps involved in Tablet Molding[9]

Advantages[9]

- Moulded tablets result in highly porous structure which increases the dissolution and disintegration rate of the product (thereby enhanced bioavailability).
- Improved mouth feels offered by water-soluble ingredients (saccharides).
- Can load high dose.
- Molded tablets are very less compact than compressed tablets.

Disadvantages[9]

- High cost of production.
- It results in erosion and breakage during handling due to its low mechanical strength.

3. Spray Drying[19,22]

In this technique supporting agent, matrix forming agents, super disintegrants and bulking agents are used i.e. gelatin can be used as a supporting agent and as a matrix, cros-povidone or sodium starch glycolate or croscarmellose are used as super disintegrants and mannitol can be used as a bulking agent. It has been reported that the tablets prepared by using the spray-dried powder should be disintegrate in less than 20 seconds in an aqueous medium. Rapid disintegration and enhanced dissolution are achieved by using the spray dried powder which is compressed into tablets.

4. Direct Compression (DC)[19,23]

DC is the simplest and most effective tablet manufacturing technique for oral dispersible tablets (ODTs) as they can be fabricated using conventional tablet manufacturing and packaging machinery and also due to the availability of tableting excipients with improved flow, compressibility and disintegration properties, especially tablet disintegrants effervescent agents and sugar-based excipients. Figure 4 shows the steps of direct compression.

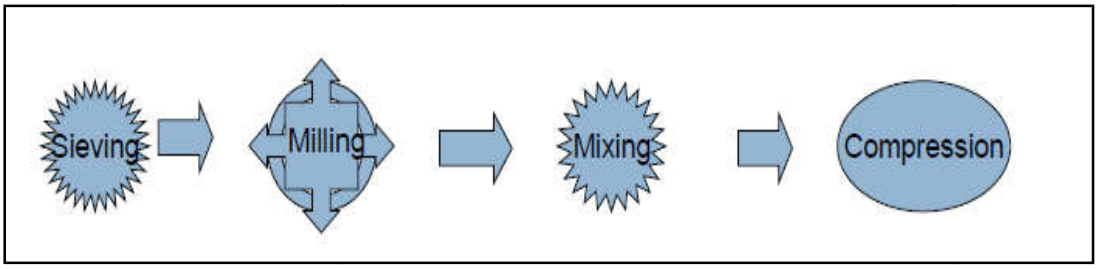

Figure 4: Steps for Direct Compression[19,23]

Advantages

- High doses can be accommodated.
- The easiest way to manufacture the tablets.
- Conventional equipment and commonly available excipients are used
- A limited number of processing steps are involved.
- Cost-effectiveness.

5. Sublimation[3,22]

Sublimation with high porosity used to produce an oral dispersible tablet. Tin this we create a porous matrix, the volatile ingredients along with other excipients into tablets, which are finally subjected to a process of sublimation. For this purpose insert, solid ingredients with high volatility (e.g. ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, naphthalene, urea, urethane, and phthalic anhydride) have been used. This volatile material is then removed by sublimation leaving behind a highly porous matrix. Tablets manufactured by this technique have reported to usually disintegrate in 10-20 sec. Even solvents like cyclohexane benzene can be used as pore forming agents. Figure 5 shown the steps involved in sublimation.

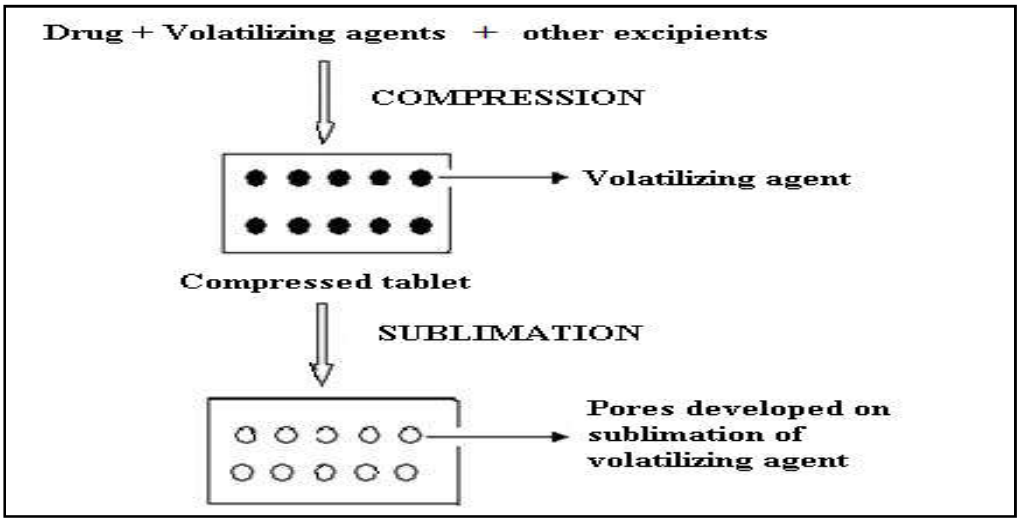

Figure 5: Steps involved in sublimation process[3,22]

6. **Mass-extrusion technology**[3,20]

Using the solvent mixture of water soluble polyethylene glycol (PEG) and methanol this technology involves softening the active blend and through the extruder or syringe expulsion of softened mass to get a cylindrical shaped extruder using the heated blade to cut into even segments to form tablets. To mask the taste this process can also be used to coat granules of bitter drugs.

7. Melt Granulation[24]

By melts granulation or wet granulation this involving the use of a hydrophilic waxy binder (Super polystate, PEG-6-stearate). Super polystate is not only acted as a binder and increase the physical strength of tablets. It is a waxy material with a melting point 33-37°C and a hydrophilic to lipid balance (HLB) value of 9. According to the conventional hot melt procedure, we used high-speed blade mixer at 40-44°C and granules were prepared. Then, granules were blended with croscarmellose, aspartate, and magnesium stearate and compressed into tablets. The melt granulation oral dispersible tablets had better hardness results than the wet granulation oral dispersible tablets. The disintegration times of melt granulation tablets, however, was more than 1 min.

8. Phase transition process[11,25]

In this process, tablets were prepared by compressing a powder containing two sugar alcohols, erythritol and xylitol and subsequent heating at a temperature between their melting points (at about 93°C for 15 min). Because of low compatibility, tablets do not have sufficient hardness. After the heating process tablet hardness is increased due to an increase of inter-particle bonds. Tablets containing about 5% xylitol showed the hardness of 4 Kg and an oral disintegration time of <30 sec.

9. Cotton Candy Process[22]

This process is so named as it having a unique spinning mechanism to produce the floss-like crystalline structure. The floss is a fibrous material similar to cotton-candy fibers, commonly made of saccharides such as sucrose, dextrose, lactose, and fructose etc. The tablets manufactured by this process are highly porous in nature and offer very pleasant mouth feel due to fast solubilization of sugars in presence of saliva. Steps involved in this process are shown in figure 6.

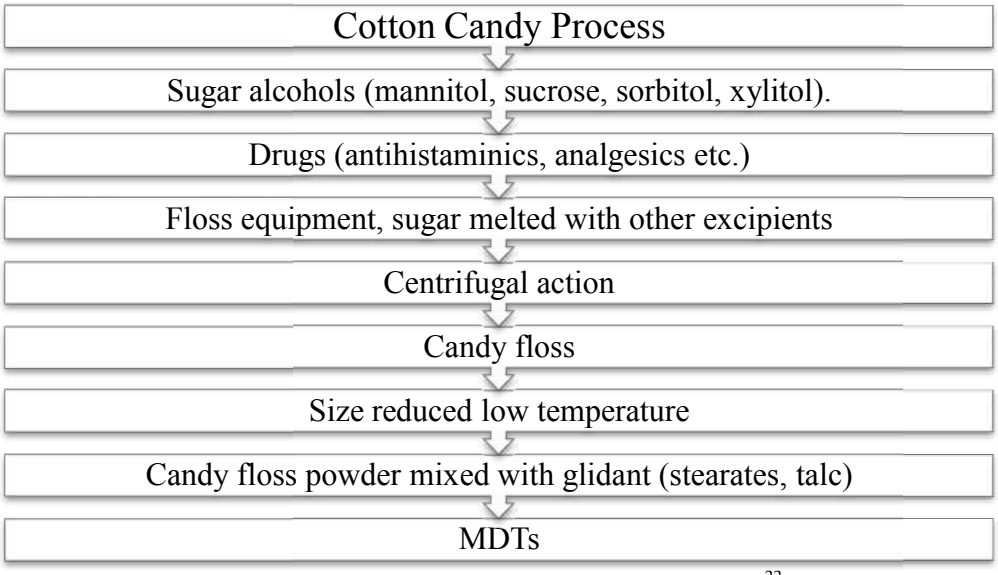

Figure 6: Steps involved in cotton candy process[22]

10. Nanonization[20]

In this technique, we reduce the particle size of the drug to nano size by using the wet milling technique. The nano crystals of the drug are stabilized against agglomeration by surface adsorption on selected stabilizers, which are then incorporated into oral dispersible tablets. This technique is mainly advantageous for poorly water soluble drugs. Other advantages are cost effective manufacturing process and include fast disintegration or dissolution of nanoparticles most important to absorption and higher bioavailability and reduction in dose.

OVERVIEW OF TASTE

Taste can be defined as a chemical reaction derived from sensory responses from the four main perceptions: salt, sour, bitter and sweet. Two other perceptions (umami and trigeminal) should be included when considering taste. Umami is derived from the presence of glutamate. Humans and others animals perceive their environment through taste which is one of the most important senses of the body. Bitter taste is one of the primary taste qualities, a sensation that arises when specialized receptors in the tongue detect specific chemicals. Figure 7 shows the taste receptors.[26]

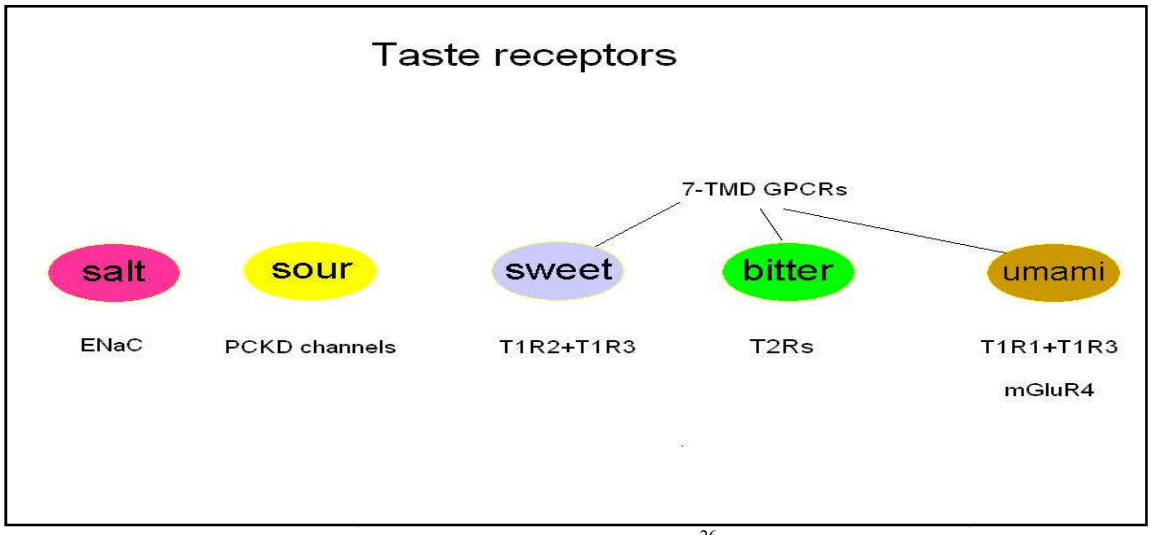

Figure 7: Taste receptors[26]

Physiology of Taste

It is important to know the basic functions of the gustatory system in order to develop effective strategies for masking the bitter taste of medications. In physiological terms, taste buds give the sensory response due to the chemical stimulation on the tongue and this sensory response is called taste. The sense of taste is conducted to the brain this process is called taste transduction. In this process when the (food or medicine) interacts with the taste receptor cells present in the taste buds.[28]Mushroom shape specialized structures called papillae on the tongue and this all are the isolated taste buds and this is spread on the surface of palate and throat.[27] For activation of ion channels, the second messenger is helpful (which includes calcium channels within the cell, and sodium, calcium and potassium channels on the extracellular membrane). It shows results in depolarization of the cell and it is important to the release of neurotransmitters that send a nerve impulse moving the signal of taste to the brain[28]. Our brain observed four different types of taste are sweet, sour, bitter and salty due to the taste buds. These feelings are reduced by the tongue and elucidate by the brain[28]. The functioning of taste buds is shown in Figure 8.

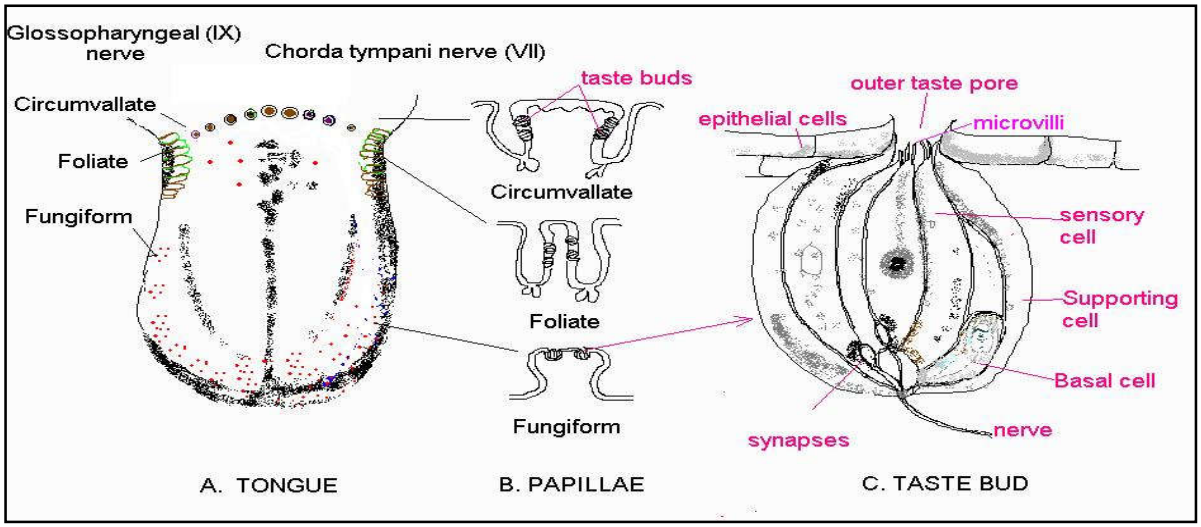

Figure 8: Physiology of taste[28]

Significance of taste masking

***"Taste masking** is defined as a perceived reduction of an undesirable taste that would otherwise exist"*. Taste is one of the most important parameters leading patient compliance. A wide variety of active pharmaceutical agents exhibits the bitter taste gave result poor patient compliance. Although the poor drug compliance due to the bitter tasting oral drugs is true for all patient populations, bit is significance for paediatric and geriatric medications. The poor palatability and bitter taste were found to be of the main reasons for noncompliance.[29]

Techniques of taste Masking[30]

1. Flavouring and sweetening agents addition
2. Ion exchange resin
3. Adsorption
4. Granulation
5. Microencapsulation
6. Pro-drug approach
7. Bitterness inhibitor
8. Solid dispersion system
9. Gel formation

1. Taste masking with flavors and sweeteners

Masking of bitter taste by use of sweeteners is the simple approach. It is not useful for highly bitter drugs. Sweeteners and flavors are generally being used along with other taste masking techniques to improve the efficiency of this technique. Due to the cooling effect of some flavoring agents it reduces the perception of bitterness. That's why a wide range of alternative sweeteners in the market today. Synthetic sweeteners such as aspartame and sucralose are commonly used in most taste masked products. Recently, sweeteners of plant origin, such as stevia

and glycyrrhizin have emerged as a viable alternative to the artificial sweeteners. Table 3 shows list of commonly used sweeteners and their relative sweetness[28].

Table 3: List of commonly used sweeteners and their relative sweetness[28]

Sweetening Agent	Relative Sweetness	Comments	Solubility
Aspartame	200	Less stable in solution	Slightly soluble in ethanol
Acesulfame Potassium	137-200	Bitter in higher concentration	Slightly soluble in ethanol
Glycyrrhizin	50	Moderately expensive	Soluble in water and alcohol
Mannitol	0.60	Negative heat of solution	Soluble in alkali
Saccharin	450	Unpleasant aftertaste	Rapidly soluble in dilute ammonium solution
Sucrose	1 (standard)	Most commonly used	Soluble in water
Stevia	300	Artificial sweetener	Soluble in water and ethanol
Sucralose	600	Synergistic sweetening effect	Freely soluble in water, ethanol and methanol

2. Taste masking by microencapsulation[28]

It is a process in which very small droplets or particles of liquid or solid material are coated with a film or polymeric material to mask the taste of bitter drugs and to achieve superior bioavailability. Gelatin, povidone, HPMC, ethyl cellulose and carnauba wax are used as covering agents for microencapsulation. Due to the coating of polymer film at active drug can reduce its solubility and taste could be masked.

Types of microencapsulation[28]

Air-suspension coating

The air suspension coating process can be described as an upward moving, expanded, fluidized bed in the central portion of the coating chamber coupled with a downward-moving, more condensed fluidized bed on the periphery of the column. Three types of air suspension coaters are available, that is top spray coater, Wurster bottom spray coater, and a tangential spray coater.

Coacervation-Phase Separation

Coacervation-Phase Separation involves following three steps.

- **Formation of three immiscible chemical phases**:- The first step involves the formation of three immiscible chemical phases: a core material phase, a liquid vehicle phase and a coating material phase. By dispersing the core material in a solution of the coating polymer, the vehicle phase is used as a solvent for the polymer the three phases are formed. By using one of the phase separation coacervation method i.e.by adding a solution, by inducing a polymer-polymer interaction and by changing the temperature of the polymer solution, the coating material phase consists of a polymer in a liquid phase is formed.
- **Core material phase**:- The process consists of depositing the liquid polymer coating upon the core material. This is accomplished by controlled, physical mixing of the coating material and the core material in the manufacturing vehicle. If the polymer is absorbed in the interface formed between the core material and the liquid vehicle phase around the core material deposition of the liquid polymer coating occurs and this adsorption phenomenon isessential for the effective coating.
- **Coating material phase**:- By using cross-linking or desolvation and thermal techniquesrigidizing the coating occurs to form the self-sustaining microcapsule.

Solvent evaporation

The microspheres were obtained by using a magnetic stirrer in the solvent evaporation method. In the organic Phaseat first, drug and Polymer were perfectly weighted and dissolved in the solvent, shook well and sonicated for 15 minutes and in the aqueous phase emulsifying agent was accurately weighed and dissolved in 100 ml distilled water. After that organic phase was injected into aqueous phase at a low stirring speed (200-600 rpm) of the mechanical stirrer for about 1 h until all the solvent evaporated. Microspheres were separated by the following filtration through a whatmann filter paper and the microspheres were dried at room temperature for 24 h. Dried microspheres were stored at 37ºC.

Spray drying and spray congealing

These both processes involve in a liquefied coating substance dispersing the core material and, spraying the core coating mixture within some environmental condition. Whereby, rapid solidification (and formation) of the coating is affected in this process. Between these two methods the main difference is the means by which coating solidification is proficient.In the case of spray drying coating solidification is effected by rapid evaporation of a solvent in which the coating material is dissolved. The coating solidification in spray congealing methods is achieved by thermally congealing a molten coating material or by solidifying a dissolved coating by introducing the coating - core material mixture into a non-solvent is accomplished. By sorption, extraction, or evaporation techniques from the coated product removal of the non- solvent or solvent is then accomplished.

Multi orifice-Centrifugal process

Varied size ranges of solids and liquid with diverse coating materials are microencapsulated by multi orifice-centrifugal process. The processing variables in this process are; concentration and viscosity of the coating material, the rotational speed of the cylinder, surface tension of the core material and the flow rate of the core and coating materials.

Pan coating

For forming small, coated particles or tablets, among industrial processes, the pan coating is the oldest and widely used process in the pharmaceutical industry. While the coating material is applied, the particles are dropped in a pan or other device. In paediatric and geriatric formulations, the problem of the bitter and obnoxious taste of drug is a challenge to the pharmacist. Masking the bitter taste of drug becomes essential in order to ensure patient compliance. With taste receptor on the tongue molecule interacts to give bitter, sweet or other taste sensation when they dissolve in saliva.

Interfacial polymerization

The reaction of monomeric units occurs between the core material and the continuous phase at the interface. The core material is dispersed in the continuous phase. The continuous or core material supporting phase may be liquid or gas and the polymerization reaction occurs at a liquid-gas, solid-liquid, liquid-liquid or solid-gas interface[31]

3. Taste masking using ion exchange resin[27,28]

Ion exchange resins are synthetic inert organic polymers consisting of a hydrocarbon network to which ionizable groups are attached. They have the ability to exchange their labile ions for ions present in the solution with which they are in contact. The most frequently employed polymeric network used is a copolymer of styrene and divinyl benzene (DVB). Apart from this other polymer such as those of acrylic and methacrylic acid cross-linked with DVB and containing proper functional groups, have been used as ion exchange drug carriers.

4. Granulation[27,28]

Granulation is a less expensive, rapid operation and an easy taste making technique. It is the common steps used in the production of tablet dosage form. Some saliva-insoluble polymers are used as binding agent. Using the polymers granules were prepared which show less solubility in saliva and thus effectively mask the taste. The effective surface area of the bitter substance is lowered by granulation that upon oral administration comes in contact with the tongue. Taste masked granules can be prepared by saliva-insoluble polymer and we can formulate the various type of tablet dosage forms with the help of taste masked granules. e.g chewable tablet, orally disintegrating tablet etc.

5. Adsorption[28]

The less saliva soluble versions of bitter drugs can be considered as adsorption of these drug. In the process of adsorption a solution of the drug is prepared by mixing it with an insoluble powder that will absorb the drug then removing the solvent or dried and used in the preparation of the final dosage

form. For the preparation of adsorbate of bitter drugs, many substrates like silica gel, vee gum, bentonite and silicates can be used.

6. Prodrug approach[27]

A medication that is administered in an inactive form or less than fully active form, which through a normal metabolic process, converted to its active form i.e. hydrolysis of an ester form of the drug is called prodrug approach.

For reducing solubility, improving taste and including prodrug design, is an effective chemical modification method. The chemically modified inert drug precursor which liberates the pharmaceutically active parent compound upon biotransformation is also the prodrug. By changing the molecular configuration of the parent molecule, the magnitude of a bitter taste response or taste receptor-substrate adsorption constant may be modified. Depending on its ultimate use the approach of prodrug can be used to increase or decrease the solubility of a drug. Making a less soluble prodrug (to mask taste) may result in compromised bioavailability is the main disadvantage. There are many examples where solubility needs to be increased. The primary examples involve drugs whose solubility is so low that a solution dosage form for intravenous usage is not possible.

7. Bitterness inhibitor[21]

In the fields of taste physiology, for bitter taste of drugs, the development of a specific universal inhibitor has been widely required. In the discovery of universal inhibitor for bitter taste one difficulty is that a substance that inhibits bitterness of one compound will not influence the bitterness of a second compound because bitterness is imparted by many different classes of compound.

By using lipoprotein, the bitter taste of caffeine, brucine, chloride, theophylline, denatonium benzoate, berberine, L-phenylalanine, naringin, propranolol hydrochloride, glycyl-L-leucine, quinine hydrochloride and strychnine nitratehave been suppressed.

8. Multiple emulsion techniques[32]

This is the new technique used to mask the taste of bitter drugs. Multiple emulsions can be prepared by dissolving the drug in the inner aqueous phase of w/o/w emulsion under the condition of good shelf stability. So that release of drug through oil phase takes place in gastrointestinal media.

The w/o/w or o/w/o type multiple emulsions are vesicular systems in which active ingredients can be entrapped in the internal phase. The entrapped substances can be transferred from internal phase to external phase through the 'membrane phase'. This phase controls the release of drug from systems.

This system could be used for controlled -release delivery of pharmaceuticals. If the system is stable enough for a reasonable shelf-life, the formulation could also mask the taste of the drug. Both w/o/w and o/w/o multiple emulsions of Chloroquine phosphate have been prepared and reported to be partially effective in masking the bitter taste of the drug.

The major problem as regards stability is the presence of two thermodynamically unstable interfaces. Two different emulsifiers are necessary for their stabilization, one with a low HLB for the w/o interface and the second one with a high HLB for the o/w interface. There are several approaches to overcome instability and release problems in double emulsions.

9. Gel formation[33]

Water insoluble gelations on the surface of a tablet containing bitter drug can be used for taste masking. In presence of bivalent metal ions sodium alginate has the ability to cause water insoluble gelation. By applying an under coat of sodium alginate and overcoat of calcium gluconate, tablets of amiprilose hydrochloride have been taste masked.

10. Taste masking by using effervescent agents[33]

For oral administration of drugs effervescent agents have advantageous and used as taste masking agents for dosage forms that are not dissolved in water prior to administration. To supply the medicament to the oral cavity for local application or for buccal absorption a chewing gum composition of bitter medicament was formulated. It comprises an orally administrable medicament, a chewing base, a taste masking generator of carbon dioxide, and optionally a taste bud desensitizing composition (e.g., oral anaesthetic such as benzocaine) and other non-active material or excipients i.e. sweeteners, flavouring agents and fillers. Recently, to supply these drugs to the oral cavity for buccal, sublingual, and gingival absorption effervescent tablets of fentanyl and prochlorperazine were developed. To promote their absorption in the oral cavity and to mask their bitter taste the formulations contain the drug in combination with an effervescent agent. For further

promotion for absorption an additional pH adjusting substance was also included in fentanyl formulation.

Selection of drugs for ODT formulations

Criteria for Drug Selection

The ideal characteristics of a drug for ODT include[16,34]

- The drug should be small to moderate molecular weight.
- Stability in water and saliva should be good.
- The drug should be partially non-ionized at the oral cavities pH.
- The drug should have the ability to diffuse into the epithelium of the upper GIT (log P >1, or preferably > 2).
- The drug is having the ability to saturate oral mucosal tissue.
- The dose of the drug should be low.

Unsuitable drug characteristic for ODTs[35]

- Short half-life and repeated dosing.
- Unacceptable taste or very bitter because taste masking cannot be achieved in that particular means.

CONCLUSION:

A new generation formulations provide the simplicity of a tablet formulation and also provide the fast action by dispersing fast or such conventional tablet formulations are oral dispersible tablets. Many techniques have been reported for the formulation of ODTs as well as many techniques have been developed for the taste masking of drug because the bitter taste of drug is the major challenge for this type of formulation.

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