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Review Article

Orodispersible Dosage Form: Advancement and Challenges

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ABSTRACT

It is challenging tasks for formulation scientists to develop paediatric formulations for all age ranges. Delivery of drugs by oral route is safest, most convenient and most economical method of drug delivery. Orodispersible tablets, Orodispersible films, fast caps, freeze dried wafers, medicated chewing gums, medicated chocolates and medicated gels and jellies are some examples of orodispersible dosage forms. Orodispersible tablets provide the rapid dissolution or disintegration of tablets when placed in the mouth. Orodispersible film quickly disperses or disintegrates in the mouth when placed onto the tongue without a need of water within few seconds. Medicated chewing gum, Gels, Jellies, soft chews offers a highly convenient patient compliant way of dosing medications for normal as well as special population groups with swallowing difficulties such as paediatrics. A new type of fast disintegrating drug delivery system such as Fastcaps, freeze dried wafers are also used now a days. Medicated Chocolate prepared by using chocolate base and the drug is incorporated into prepared chocolate base. This article defines the various types of orodispersible delivery system, its benefits, disadvantages, challenges also, reviews and compares various orodisperse dosage forms.

keywords: Orodisperse, Mouth dissolving, Merdicated chocolate, Paeditrics, Mouth dissoving film

1. INTRODUCTION

Undoubtly, oral route is the most preferred route of drug administration both for solid and liquid dosage forms. However, solid dosage forms such as powders, tablets, capsules are popular because of the ease of administration, accurate dosing, self medication, and ultimately compliance of patient. Drinking water is must for the oral administration of drugs however, many people suffering from dysphasia and especially with pediatric finds it difficult in swallowing

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tablets and capsules, which results in high incidence of noncompliance and ineffective therapy [1].

Children differ from adults in many aspects of pharmacotherapy and it is a challenging job for formulation scientists to develop pediatric formulations for all age ranges (neonates, toddlers, young children and adolescents) which includes acceptable dose volumes and sizes, safety (choking for solid dosage forms),varying needs and bitter taste. It is the need of an hour that pediatric medicines are formulated to best suit a child's age, size, physiologic condition, and treatment requirements.

Advancement in the formulation and technological development resulted in some recent progress in the development of pediatric formulations, such as greater dose flexibility, easier administration, and better acceptance of drug formulations in children [2].

Orally dispersible systems (OD's) have imprint forte amongst the oral delivery systems due to great level of patient compliance and some additional advantagesspecially with paediatrics. They are solid dosage forms, which dissolvers or disintegrate in the mouth within a minute in the presence of saliva. From last few decades, OD's have received ever increasing demand and has become a rapidly growing area in the pharmaceutical industry [3].

Types of orodispersible dosage forms

Orally disintegrating dosage forms are manufactured by various technology such as Direct Compression, Freeze Drying or lyophilization, Molding, Disintegrant addition, Sublimation, Spray Drying, Mass Extrusion, Cotton-candy process, Nano Crystal Technology[4].The development of an OD's requires specialized manufacturing methods and/or particular excipients[5].

Different orally disintegrating dosage forms are as follows:

1. Orally disintegrating tablets
2. Fast dissolving films
3. Orodispersible granules
4. Medicated chewing gums
5. Freeze-dried wafer
6. Medicated gels and jellies
7. Medicated chocolate

Orally disintegrating tablets (ODTs**):**

ODTs are a solid dosage form that provides the rapid dissolution or disintegration of tablets when placed in the mouth [6].ODTsare also known as orodispersible tablets, quick disintegrating tablets, fast disintegrating tablets, mouth dissolving tablets and rapid melts.

These are tablets which get dispersed or disintegrate when gets in a contact with saliva with the release of active drug providing maximum drug bioavailability as compared to conventional dosage form. Superdisintegrants can be added in the formulation which helps in fast releases of drug in mouth increasing the bioavailability [7].

The fast disintegrating property of the tablet is attributable to a quick ingress of water into the tablet matrix resulting in its rapid disintegration. Hence, the basic approaches to develop rapidly dissolving oral dosage forms include maximizing the porous structure of the tablet matrix, incorporating the appropriate disintegrating agent and using highly water soluble excipients in the formulation[8].

Advantages of orally disintegrating tablets

The advantages of ODT include [9-11]:

- Easy to swallow.
- No need of water to swallow the tablet.
- Better stability.
- Easier production process.
- Convenient for the use of the patients.
- Pleasing mouth feel and taste (palatability).
- Easy administration for paediatric, elderly and mentally disabled patients.
- No residue in the oral cavity after administration.
- Allow high drug loading.
- Accurate dose (as compared to liquids).
- Rapid onset of action.
- Easy Transportation.
- Reducing first pass metabolism, which offers improved bioavailability as, some amount of drugs is absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach.
- No risk of chocking and suffocation thus offering improved safety.
- Easy to manufactured by direct compression method with low cost.

Challenges and limitations of ODTs it includes [12, 13]:

- Insufficient mechanical strength.
- The tablets may produce unpalatable taste and grittiness in the oral cavity if not formulated properly.
- Large dose drugs not preferable.
- Palatability- Most of the drugs have bitter taste.
- ODT requires special packaging for stability and safety of product.
- Drug should be stable in water and in saliva and should be able to permeate oral mucosal tissue. Stability to humidity.

Method of Preparation:

ODTs are generally prepared by, freeze-drying (lyophilization), direct compression, sublimation, spray-drying and mass extrusion method [14].

2. ORODISPERSIBLE FILM

Orodispersible Film (ODF) is also known as Fast dissolving film, fast disintegrating film, and mouth dissolving film. ODFs are postage stamp sized strips of thin polymeric films prepared to quickly disperse or disintegrate in the mouth when placed onto the tongue without a need of water within 1 to 30 seconds [15].

ODFs dissolves or disintegrate rapidly when placed on the floor of the tongue and release the medication for local and/or systemic absorption [16].Local delivery has a number

of applications such as, treatment periodontal disease, bacterial and fungal infections. For the treatment of chronic diseases, the mucoadhesive film allows easily accessibility and for administering drugs by systemic action [17].

ODFs have all the advantages of solid dosage form such as, precise dosage, easy administration and of liquid dosage forms such as, easy swallowing, palatability and rapid bioavailability [18].

Advantages [18]

ODFs have all the advantages of solid dosage form such as, precise dosage, easy administration and of liquid dosage forms such as, easy swallowing, palatability and rapid bioavailability. Orodispersible films (ODFs) possess potential to facilitate oral drug delivery to children

The advantages are:

- Improved patient compliance.
- As fast dissolving thin oral films are flexible, they are easy to carry, store and handle, which is not the case with orally disintegrating tablets (fragile and brittle).
- Precision in the administered dose is ensured from each of the strips as compared to drops or syrup formulations.
- Water is not needed for administering, so problem encountered in swallowing of tablets or capsules can be evaded.
- Patients suffering from repeated emesis, dysphagia, motion sickness prefer this dosage form as they are unable to swallow large quantity of water.
- Availability of larger surface area leads to fast disintegration and dissolution in the oral cavity.
- As the oral mucosa is being highly vascularized, drugs directly enter the systemic circulation without undergoing first-pass hepatic metabolism. This results in improved oral bioavailability of molecules.
- These films can be manufactured through economically feasible nonsophisticated procedures and uncomplicated equipment.

Disadvantage [19]

- High dose cannot be incorporated into the film.
- ODFs are thin which requires specialized, storage, handling and packaging.
- A general major drawback of ODFs is taste. Bitter drug needs taste masking which may reduce maximum drug load.

SPECIAL FEATURES OF FAST DISSOLVING FILMS

An ideal ODF should be [20-22]:

- Available in various size and shapes.
- Thin and Flexible.
- Unobstructive.
- Transportable.
- Acceptable taste and a pleasant mouth-feel.
- Ease of handling and administration.
- Adhere to the oral cavity easily.
- Disintegration time should be as short as possible.

Challenges in formulation development of fast dissolving oral films [23]:

Following are some of the challenges in formulating fast dissolving oral film:

- Insolubility of drug
- Taste masking of bitter drug
- Reduction in drying time of film
- High dose Loading in film
- Co administration of two or more drugs
- Stability of film against humidity and temperature
- Need special packaging

Manufacturing Methods:

The general polymeric carriers used in ODF formulation are cellulose, starches, gums and polysaccharides , and semi-synthetic or synthetic polymers. Other functional excipients included in the films are: humectants, saliva stimulating agents, sweeteners, permeation enhancers and colouring/flavouring agents [24].

The manufacturing of orally dissolving films can be done by various methods such as [25-27]:

1. Solvent casting method
2. Hot melt extrusion method
3. Semisolid casting method
4. Rolling method
5. Solid dispersion extrusion
6. Electrospinning of drug-loaded polymeric solutions

3. MEDICATED CHEWING GUMS

Medicated chewing gum (MCG) are solid single dose preparations with a base consisting mainly of gum that are intended to be chewed providing a slow and steady release of the medicine [28]. This offers a highly convenient patient compliant way of dosing medications for normal as well as special population groups with swallowing difficulties such as pediatrics. Chewing gums are not meant to swallow and the remaining mass after chewing is discarded. During chewing the drug contained in the gum is released into the saliva and offer both local and systemic effect [29].There are various factors that influence the release and absorption of the drugs, for example, rate and intensity of chewing and the amount of saliva that is produced [30].

ADVANTAGES [31-34]:

The advantages may be summarized as bellow:

- Chewing gum can be used without water, at any time, and everywhere.
- Fast/rapid onset of action
- Ready to use
- High bioavailability
- Pleasant taste
- Ready for use
- High acceptance by children and for patients who find swallowing tablets difficult
- Effect on dry mouth (xerostomia)
- Offers distinctiveness

- Less first-pass metabolism and improved bioavailability
- Increase the rate of saliva secretion. Stimulated saliva has a buffering capacity

Disadvantages of Chewing Gum [35]

- Frequent gum chewing may result in attrition of teeth also cause dental erosion.
- Prolong chewing on gum may result in pain in facial muscles and earache in children.
- Chewing gum may irritate the digestive system, leading to stomach aches.
- Children less than six years of age may get choked on swallowing a gum.
- Control over drug release is erratic

Manufacturing of CGS:

Chewing gum is a combination gum base and other excipients include Bulking agents (guar gum hydrolysates, dextrin, polydextrose, inulin), humectants (Glycerine), softeners (glycerin, lecithin), Sweetening agents (sorbitol, corn syrups, Sugar and sugar alcohols),Glidants (Colloidal silica,) colours, flavours and preservatives [36].

Medicated chewing gums can be manufactured by [37]:

1. Conventional/traditional method (Melting)
2. Freezing, grinding, and tableting method
3. Direct compression method.

Factors Affecting Release of Active Ingredient

1. Contact Time
2. Physicochemical properties of active ingredient.
3. Inter individual variability.
4. Composition and amount of gum base affect rate of release of active ingredient. If lipophilic fraction of gum is increased, the release rate is decreased [38].

Fast disintegrating capsules (Fast Caps):

A new type of fast disintegrating drug delivery system based on gelatin capsules was developed. In contrast to conventional hard gelatin capsules, the fast caps consist of gelation of low bloom strength and various additives to improve the mechanical and dissolution properties of capsule shell. Fast disintegrating capsules are generally prepared by dipping process, perforation or by vacuum-drying of conventional hard capsules [39].

The mechanical properties of fastcaps found to be same as that of gelatin capsules, which assures good process ability and handling [40].

Advantages:

- High drug loading
- solid and liquid filling possible,
- No Compression Steps
- Easy to manufacture

Challenges:

- Moisture sensitive drug difficult to prepare
- Requirement of special packaging.

4. FREEZE-DRIED WAFER

Freeze dried wafer is a fast disintegrating, thin matrix containing drug dissolves in oral cavity or swallowed without water. The wafer disintegrates instantaneously in the oral cavity and releases drug, which dissolves or disperses in the saliva. The saliva is swallowed and the drug is absorbed across the gastrointestinal tract (GIT). [41] The Wafertab filmstrip can be flavoured for taste masking and increasing the palatability. It is available in different shapes and sizes and is an ideal method for delivery of drugs, which require fast release or for use by patients who have difficulty in swallowing [20]. Freeze-dried formulations have low water content, and do not support microbial growth. Oral lyophilized wafers contain taste masking agents, lyoprotectors, and pH adjusters along with the Sweeteners to mask unpleasant taste and are essential for patient compliance [42].

5. MEDICATED GELS AND JELLIES

Jellies are translucent, transparent or non-greasy semisolid preparations meant for external and internal applications. Medicated Jellies meant are drug containing gelatinous preparations of definite size and shape, meant for oral administration. Medicated jelly oral dosage forms are more suitable for pediatric, geriatric and patients with dysphagia. jellies candies are easily accepted by children as they enjoy the taste and the chewing property of the jellies because they are often flavoured with fruit juices, extracts and have sweetness property.

MJs are mainly used over mucous membrane and skin and they possess local anaesthetics and antiseptic properties. These jellies hold adequate amount water which after evaporation gives a local cooling effect and residual film provides protection. Example: Ephedrine sulphate jelly is used to seize the bleeding of nose since it is vasoconstrictor

Development of this type of formulation increase in bioavailability, helps to bypass extensive hepatic first pass metabolism, reduction of dosage wastage, dose dumping, stability and taste masking [43].

Advantages of gels and jellies [44]**:**

- Easy to administer.
- Can be administered to person found difficulty in swallow such as paediatrics, geriatric and psychiatric patients.
- Provides convenience and patient compliance especially for travelling.
- High drug loading.
- No risks of chocking or suffocation, due to smoothness.
- Improved taste masking and good mouth feel property
- Stimulates salivation facilitates swallowing.

Disadvantages of gels and jellies [44]**:**

- Chance of microbial contamination.
- Dose uniformity is a problem.

- Packing of these dosage forms has to be done properly to prevent exposure from light, spillage during travelling.
- Bitter taste drug may dose problem.

Manufacturing of Medicated Gels/Jellies:

Various Components of Medicated Jelly Formulation are depicted in Table No.1

Table 1: Manufacturing composition of medicated jellies

Ingredients	Examples
Gelling Agent	Gellan Gum, Gelatin, Xanthangum, Sodium alginate, Pectin, tragacanth, Carrageneen, MCC
Stabilizers	Propylene Glycol, Sorbitol, Chelating agent: To prevent the sensitivity of bases EDTA should be used
Stabilizers	Methyl Paraben, Chlorhexidne acetate, Propyl Paraben, Benzalkonium Chloride, Sodium Benzoate.

6. SOFT CHEWS

Soft chew are defined as solid or semi solid dosage form containing water soluble excipients with one or more active pharmaceutical ingredients to release the drug by chewed in between the teeth before swallowing. The proper selection of packaging material is important in soft chew to maintain the long term integrity of the formulation [45].

Advantages of Soft Chews [46]**:**

- Prefer well children
- rapid drug Absorption
- Improved bioavailability
- Fast onset of action
- Exhibits Local as well as systemic effect
- Easy to administer as it does not requires water

Disadvantages of Soft Chews [46]**:**

- Prolonged chewing can results in pain in facial muscles and ear ache in children
- Store in dry place as it is hygroscopic
- Specilized packaging is required

7. MEDICATED CHOCLATE

Chocolate is highly sophisticated a versatile food. Medicated chocolate is prepared by using chocolate base and the drug is incorporated into prepared chocolate base. As the drug is incorporated within the chocolate and the drug is released from the chocolate, it is called as Chocolate drug delivery system Chocolate is well suited as a vehicle for delivering active agents in many aspects. Chocolate abundantly contains compounds such as saturated fat, polyphenols, sterols, di and tri terpenes, aliphatic alcohols, and methyl xanthines. Cocoa is the principle ingredient of chocolate Cocoa contains more phenolic antioxidants than most foods. Flavonoids, including catechin, epicatechin, and procyanidins predominate in antioxidant activity [47].

Advantages of Chocolate drug delivery system

- A possible bypass of first pass effects.
- Avoidance of pre systemic elimination within the GI tract.
- High consumption of dark chocolate and cocoa is associated with reduced risk of CVD and cardiovascular mortality.
- Cocoa products are rich is plant phytochemicals, especially flavonoids, with strong antioxidant properties [48].
- Chocolate is also an anhydrous medium and is therefore resistant to microbial.
- Chocolate is well-suited as a vehicle for delivering various category of drugs.

Chocolate drug delivery system has Disadvantages

- It can cause cholesterol problem, gaining extra weight.
- Dark chocolate carries as much caffeine causes dehydration which affects our digestion system.
- Formulation is patient specific (Calorigenic).
- Heat labile drugs cannot be used in this formulation because of the high temperatures required for preparation.
- Bitter drug not suitable.

Method of Preparation of Medicated chocolate:

The medicated chocolate was prepared by using and ng compound chocolate and cocoa powder along with the other ingredients by fusion techniques.

TYPES OF CHOCOLATE

Various types of chocolates are available as, Sweet Chocolate, Couverture, Milk Chocolate, White chocolate, Milk Chocolate Couverture on the basis of various percentage of total cocoa solids, cocoa butter and fat-free cocoa solids [49].

Challenges for preparing the medicated chocolate:

Chocolate is also an anhydrous medium and is therefore resistant to microbial growth and to hydrolysis of water-sensitive active agents.

8. SUMMARY AND CONCLUSION

Many people suffering from dysphasia and especially with pediatric finds it difficult in swallowing tablets and capsules, which results in high incidence of noncompliance and ineffective therapy. Orodispersible dosage forms have potential advantages over conventional solid dosage form such as, improved patient compliance, convenience, greater bioavailability, and rapid onset of action. From last few decades, OD's have received ever increasing demand and has become a rapidly growing area in the pharmaceutical industry.

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