A review on recent trends in oral drug delivery- lyophilized wafer technology

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Abstract : The lyophilized wafer technology is an effective and versatile drug delivery system for oromucosal application. This has been established from the extensive physicochemical and physicomechanical profiling conducted. Due to small size, little dose, thickness of buccal wafer over other dosage form is most acceptable and pleasant. Flash release oral wafer drug delivery system is an alternative approach for the tablets, capsules, and liquid oral dosage forms for pediatric and geriatric patients. The wafer system containing HPC, lactose, mannitol and glycine had the ability to disintegrate within 30 seconds. The modified wafer system, consisting of pectin cross linked with zinc ions serving as the drug reservoir, and mucoadhesive polymer combination of pectin, carmellose and gelatin, provided effective release of model drug diphenhydramine hydrochloride over approximately six hours. The semi-synthetic and synthetic natural polymer as film former in low concentration can be used for the preparation of buccal wafers and hence such dosage form are easy to handle, cost effective, fast absorbable, non- irritating and mostly preferred by patient. It improve the efficacy of APIs by dissolving within minute in oral cavity after the contact with less saliva as compared to fast dissolving tablets, without chewing and no need of water for administration. Present article overview the advancement in the oral dosage forms, application, formulation composition, method of preparation, evaluation and marketed products of oral flash release wafers.

Keywords: Lyophilized, Novel Drug Delivery, Orally disintegrating tablets (ODTs), Over the Counter Products (OTCs)

INTRODUCTION

Formulation consideration Among the novel drug delivery system buccal drug delivery is the main and extensive acceptable drug delivery between the other delivery system . The innovation designs may involve modifying formulation composition and manufacturing technologies to achieve new product end point. Among the fast dissolving drug delivery system, oral flash release wafer drug delivery system is an alternative to tablet capsules and syrups for pediatric and geriatric patients who experience in difficulties of swallowing traditional oral solid dosage form. This technology has been used for local action rapid release of product and direct systemic circulation in the oral cavity to release drug in rapid fashion. The pharmaceutical wafers hold potential advantages like rapid disintegration no swallowing or chewing ,no co-administration of water ,accurate dosing compared to liquid products great safety and efficacy along with the patient compliance. Buccal dosage forms include mucoadhesive tablets films patches ointments and hydrogels, each of which has limitations. Wafers products are available to patients for immediate release of several API. Wafers –an innovative oral dosage forms new oral thin films so called wafers thus creating new possibilities for action profiles and patient compliance. Wafers are paper thin polymer film used as carriers for pharmaceuticals agents.The 2008 FDA guidance recommends a disintegration time of 30 seconds or less based on Us pharmacopoeia disintegration test method and maximum tablet weight of 500mg. ODTs are preferred by multiple patients groups with swallowing difficulties , including geriatrics, dysphasic, and extension for first to market product and marketing differentiation for over the counter products.And also this delivery protect drug form first pass metabolism and improve the dissolution. Oral thin wafer drug delivery system are solid dosage forms , which dissolve in a short period of time when placed in the mouth without drinking water .These are also referred as fast dissolving oral wafers, buccal films.

The rational for development and use of novel drug delivery system may include one or more of the following arguments:

1-Decrease the toxicity and occurrence of adverse drug and metabolism in the blood at the target sites
2-Attractive dosage form with new active ingredients
3-Improve drug utilization by applying a smaller drug dose in a controlled–release form to produce the same clinical effect as a larger dose in a conventional dosage form.
4-Provide greater patient convenience and better patient compliance by significantly prolonging the interval between administrations.
5-Improvement of established products
6-Provide a uniform blood concentration and or provide a more predictable drug delivery.
7-Optimization of bioavailability
8-Increase patient compliance
9-Innovative technology for product
10 -Increase of product appeal through innovative formula.
11- Exclusivity and cutting edge technology position in the market through a step forward.
12- Access to new indications by means of a new absorption profile even for existing active ingredients.

Anatomic Physiological Consideration:-

The four regions are used in the drug administration in the buccal cavity. The four regions have the high different permeability plays an important role in the absorption of drugs across the oral mucosa. The sites of drug administration in the four mentioned areas above are the sublingual and the buccal route. The anatomic site for the drug administration between the cheek and gingal area is known as the buccal mucosa. In oral mucosa three layer are present. The mucosa of the buccal and sublinal regions have only small amounts of cermide thus it is more permeability when compared to other regions of the oral cavity modification of the drugs partition coefficient can be used in some approaches.

Physicochemical Properties of the oral mucosa:-

The surface of buccal cavity comprises of satisfied squamous epithelium which is essential too separated from the underlying tissue of lamina propria and sub mucosa. it is interesting to note that the permeability of buccal mucosa is greater than that of the skin , but less than that of the intestine. Hence the buccal delivery serves as an excellent platform for absorption of molecules having poor dermal penetration. The primary barrier to permeability in the oral mucosa is the result of intercellular material derived from the so called membrane coating granules present at the uppermost200micron layer.

ADVANTAGES OF WAFERS TECHNOLOGY

1-No first pass effect
2- High dissolution due to a large surface area.
3-More patient compliance
4-Reduced impact on the gastrointestinal tract
5-Low dose can only be incorporated.
6-Discrete and easy application
7-Better durable than oral-dispersible tablets
8-No risk of choking
9-Improved bio-availability, translates to lower dose

TYPES OF WAFERS

1-Flash dissolved wafers.
2-Melt away wafers
3-Sustained release wafers.
4-Flash dispersed wafers.

OBECTIVE OF FORMULATION OF WAFERS

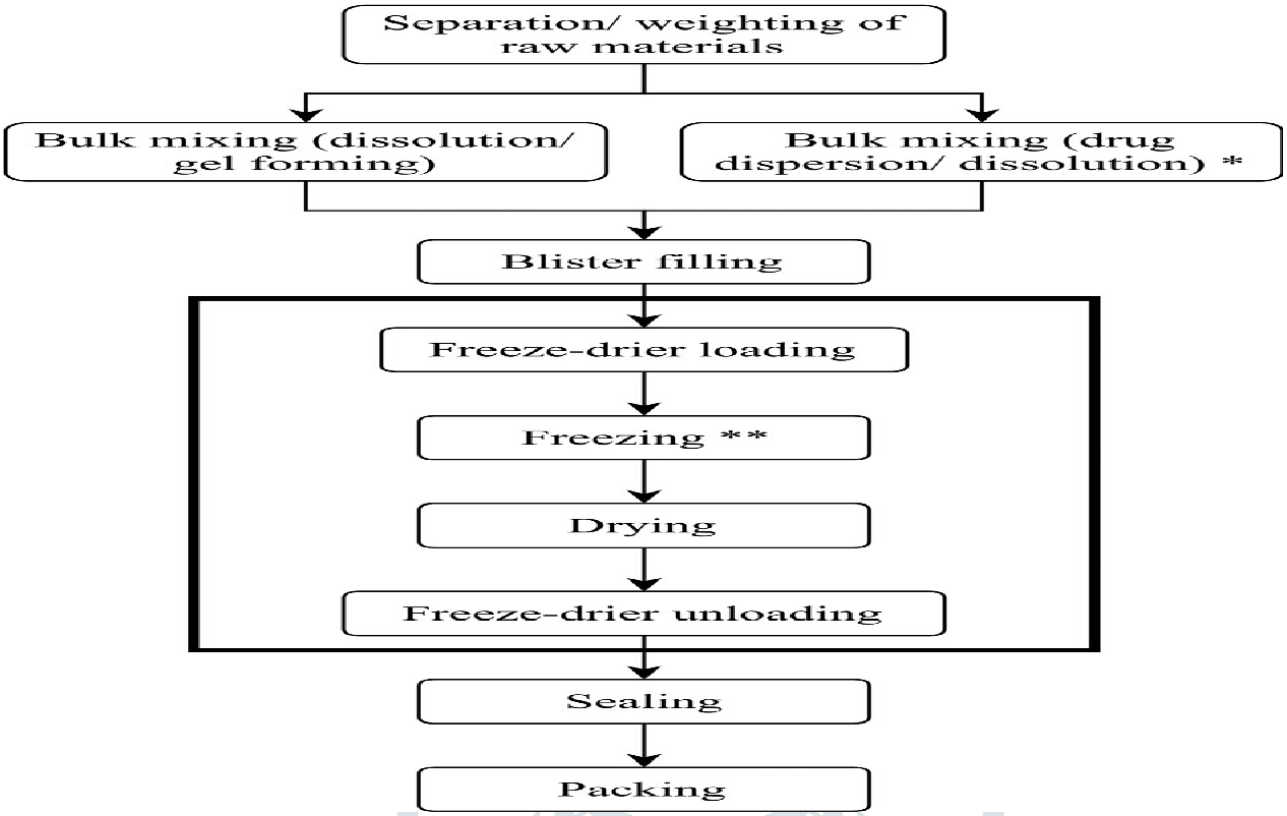
The aim of percent research work is development and characterization of mouth dissolving oral wafers of a suitable drug.
Candidate so as to achieve following objective:-
1-To improved patient compliance and provide a rapid onset of action.
2-To reduce side effect associated with the API by reducing its dose.
3- To enhance the oral bioavailability of molecules.

OPEN MATRIX –TYPES WAFERS AND TABLET

The first of this class of delivery system to be manufactured on a large scale. It was a freeze dried wafer made from various standard tablet adjuvant the wafer essentially works on the principle of forming an open network containing the active ingredient . This tablet is manufactured using conventional granulating and compression. The finished product is a porous solid capable of very rapid disintegration .The active ingredients remain in a dispersed state within the mass. The concept of quick disintegration drug delivery system gained much attention.

1-Active pharmaceutical agent -5-30%
2-Wafer forming polymers-45%
3-Plasticizer-0-20%
4-Sweetening agent-3-6%
5-Saliva stimulating agent 2-6%
6-Flavouring agent-q.s.
7-coloring agent-q.s

Production process:-



COMPOSITION OF THE ORAL THIN WAFER

Mouth dissolving wafer is a thin wafer with an area of 5-20cm containing an active ingredient. The instant dissolution in water or saliva corresponding soluble polymers. Drug can be incorporated up to a single dose of 15mg.

1-Drugs:- Different classes of drugs can be formulated as mouth dissolving wafer including anticancer e.g.-Omeprazole NSAIDS-PCM.

2-Wafer Forming Polymer:-The use of wafer forming polymers in dissolvable wafers has attracted considerable attention in medical and Nutraceutical application. The disintegration of the polymer is decreased by increasing the molecular weight of polymer wafers e.g.-HPMC, Methylcellulose, Gelatin.

3-Plasticizers:- The mechanical properties such as tensile strength and elongation to the wafers have also been improved by the addition of plasticizer. e.g.-Glycerol, polyethylene glycol etc.

4-Sweetening Agents:- Sweeteners plays important role for improving compliance wafers in pediatric population .The classical source of sweetener is sucrose, dextrose, glucose .

5-Colour:- A full range of colors is available including FD and C colors, EU colors, natural colors.

ANALYSIS OF TABLET WAFERS:-

1-Organoleptic Evaluation
2-Mechanical Properties
A-Thickness
B- Dry Test
C- Tensile Strength
D- Percent Elongation
E- Tear Resistance
3-Swelling Properties
4-Transparency
5-Taste Evaluation
6-Content Uniformity
7-Disintegration Time
8-In-Vitro Dissolution Test
9-Stability Testing

1-Organoleptic Evaluation

For evaluation of the product special controlled human taste panels are used. In-Vitro methods of utilizing taste sensors are being used for this purpose.

2-Mechanical Properties:-

Mechanical Properties of wafers are evaluated using a texture analyzer equipment equipped with a 5Kg load cell. The force and elongation were measured when wafer beaks. Three mechanical properties namely tensile, strength, elastic modules and percent elongation are calculated.

a-Thickness-

The thickness of wafers can be measured by micrometer screw gauge at different strategic locations. .The essential to ascertain uniformity in the thickness of the wafer as this is directly related to the accuracy of dose in the wafer.

b- Dryness Test:-

Dryness test is the tenacity with which the wafer adheres to an accessory that has been pressed into contact with the wafer.

c- Tensile Strength:-

It is the maximum stress applied to the point at which the wafer sample breaks. It is calculated by the applied load at rupture divided by the cross –sectional area of the wafer as given in the equation below:

Tensile Strength = (load at failure .100)/ (initial length of wafer)

d- Tear Resistance:-

Tear resistance of plastic wafer or sheeting is a complex function of its ultimate resistance rupture. Basically very low rate of loading 51mm is employed to measure the force to initiate tearing. The maximum stress or force (that is generally found near the onset of tearing) required to tear the specimen is recorded as the tear resistance value in Newton.

e:-Folding Endurance: -

Folding endurance is determined by repeated of strip at the same place till the strip breaks. The number of times the wafers is folded without breaking is computed as the folding endurance value.

3- Swelling property:-Wafer swelling study is conducted using simulated saliva solution. The wafer sample is weighed and placed in a stainless steel wire mesh. The mesh contain wafer sample is submerged into 15ml medium in a plastic container. Increase in the weight of the wafer is determined at predetermined time intervals until a constant weight is observed. The degree of swelling is calculated using formula.

A= (wt-wo)/wo)

Wt is weight of wafer at time t and Wo is weight of wafer at time zero.

4-Transparency:-The transparency of the wafers can be determined using a simple UV spectrophotometer. C the wafer samples into rectangles and placed on the internal side of the spectrophotometer cell. Determine the transmittance of wafers at 600nm. The transparency of the wafers can be calculated as follows.

Transparency = (logT600)/b=-c

Where, tT600 is the transmittance at 600nm, bis the wafer thickness, cis concentration.

5-Taste evaluation:- Taste acceptability was measured by a taste panel consisting of human volunteers with 10 mg drug and subsequently wafer sample containing 10mg drug held in mouth until disintegration , then spat out and he bitterness level was recorded The volunteers were asked to gargle with diluted water between the drug and sample administration.

6-Content uniformity:- This is determined any standard assay method described for the particular API in any of the standard pharmacopoeia. Content uniformity is determined by estimating the API content in individual strip.

7-Disintegration Time:- The disintegration time limit 30 seconds or less for orally disintegration tablets described in CDER guidance can be applied to fast dissolving oral strip. Pharmacopoeia disintegrating test apparatus may be used for this study. Typical disintegration time for strip is 5-30s.

8-In-vitro Dissolution Test:- Dissolution testing can be performed using the standard basket or paddle apparatus described in any of the pharmacopoeia. The dissolution medium will essentially be selected as per the sink conditions and highest dose of the API. Many time dissolution tests can be difficult due to tendency of the strip to float on the dissolution medium where paddle system is used.

9-Stability test: - A piece of wafer preparation was stored in an aluminum package at 25c with 50-60% humidity or at 40 with 75% humidity for 2-24.

Packaging of oral wafer:-

In the pharmaceutical industry it is vital that the package selected adequately should preserve the integrity of the product .Expensive packaging, specific processing and special care are required during manufacturing and storage to protect the dosage of other fast dissolving dosage forms. A variety of packaging options are available for fast dissolving wafers. Single packaging is mandatory for wafers. An aluminum pouch is the most commonly used packaging formula.

1-Single pouch:-

Soluble film drug delivery pouch is a peelable pouch for quick dissolve soluble films with high barriers properties. The pouch is transparent for product display. Using 2 structure combinations allows for one side to be clear and the other to use a cost effective foil laminations. The foil lamination has essentially zero transmission of both gas and moisture .The single dose pouch provides both product and dosage protection.

2-Blister card with multiple units:-

The blister container consists of two components the blister, which is the formed cavity that holds the product and the lid stock, which is the materials that seal the blister. The film selection should be based upon the degree of protection required. Generally Third lid stock is made of aluminum foil. The material used to form the cavity is typically a plastic, which can be designed to protect the dosage form from moisture.

3-Polyvinyl chloride:-
The most commonly used blister materials PVC. The materials, which provides a nominal to moisture is used when the product does not require effective moisture protection.
4-Barrier Films:-
Many drug preparations are extremely sensitive to moisture and therefore require high barrier films. Several materials may be used to provide moisture protection such as Poly-chlorotrifluoroethylene film, Polypropylene.
5-Continuous Roll Dispense:-
The dispenser contains a measurement device for carefully measuring the length of tape as it dispense. A counter monitors the remaining doses of drug tape remaining within the dispenser. The administration of the dose to the patient may be set by adjusting the tape length released for each single dose and selection the time intervals between dosage. The invention comprises also ingestible tapes of medicament.

APPLICATIONS OF ORAL FILM DELIVERY SYSTEM:-
A-Taste masking:-
Taste masking of the drugs becomes critical to patient compliance because the oral film systems dissolves or disintegrate in patient s mouth, thus releasing the active ingredients which come in contact with the taste buds. An important aspect of wafer drug delivery is the masking of the often bitter and poor taste of drug formulations One method of taste masking is encapsulation the coating of drug particles with a polymeric covering sufficient to mask the taste of the drug particles while maintain the ability to release the drug for absorption.
B-Vaccination:-
Oral thin film is delivered in the form of vaccine which is stable at room temperature so that is quickly dissolves in mouth and in saliva Rotavirus vaccine is room temperature stable quick dissolving oral thin film delivery system for vaccines that will make vaccination almost as simple as freshening your breath the sustained release strip is applicable in hospital preparation and drug carriers.

CONCLUSION:-
Medicated wafers as novel drug delivery system having a better patient compliance and may offers to improving biopharmaceuticals properties, improved efficacy and better safety compared with the conventional dosage forms the flash release wafer is promising due to the availability of modern technologies combined with well built market acceptance oral wafers can replace the over the counter drugs generic & name brand from market due to lower cost and consumer compliance.

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