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Review Article

Medicated Wafers as a Novel Drug Delivery Carrier

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ABSTRACT

Pharmaceutical researchers worldwide are increasingly intrigued by the potential of medicated wafers as a groundbreaking method for drug delivery. Offering an alternative to conventional dosage forms, medicated wafers have emerged as a versatile option due to their ease of swallowing, self-administration, and rapid dissolution. These wafers can be administered via various routes including oral, buccal, sublingual, and transdermal, catering to both systemic and local interventions. However, developing effective thin wafers requires a deep understanding of the pharmacological and pharmaceutical properties of drugs and polymers, along with judicious selection of production techniques. This review aims to provide an encompassing overview of innovative formulation techniques, existing patents, pharmaceutical applications, and the key factors influencing thin wafer formulation such as the physicochemical properties of polymers and drugs, anatomical and physiological considerations, and methods for wafer characterization. Furthermore, the review discusses the latest trends and perspectives in thin wafer product design and addresses pertinent issues faced by businesses involved in thin wafer development.

Keywords: Medicated Wafers; Oral Drug Delivery; Clinical Trials; Methods of Preparation; Patents

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1. Introduction

Optimal drug therapy with a convenient dosage form is achieved by taking the right medication at the correct time [1]. The oral route is one of the most preferred drug administration routes as it is more convenient, prevalent, and cost-effective and gives a high degree of compliance with patients. Nearly 70% of formulations are forms of strong dosage. However, geriatrics, paediatrics, and bedridden patients have difficulty swallowing or chewing types of strong dosage like tablets, capsules, and pills. Due to unpleasant dosage forms, several paediatric and geriatric patients are afraid to take strong formulations [2]. There will be an immense need to develop a new dosage form to improve the drug efficiency presently on the market. As a small price, it includes both money and time to reconsider delivery approaches to improve the usefulness of drugs already authorized rather than pharmaceutical companies developing a single new chemical entity. Many pharmaceutical companies have led their research into reforming current drugs into new types of dosage [3] [4]. By formulating the drugs into medicated wafers, the above-mentioned issues could be efficiently addressed. Medicated wafers/oral films, also known as oro wafers, are a group of flat films that dissolve rapidly in the oral cavity within a second without water administration. Oral wafer delivery is a vehicle, essentially just a thin flexible sheet of polymer in which an active pharmaceutical ingredient (API) is incorporated [5]. Several wafers are intended to be quickly dissolved in the oral cavity to absorb a drug in the gastrointestinal path (oral and oral soluble, or Orodispersible wafers/films); some are ready to create a drug at the administration site (e.g., buccal, sublingual, and ophthalmic thin films). It was recognized that drugs with elevated mucosal permeability are optimal for buccal and sublingual delivery with wafers [6]. Medicated wafers that dissolve quickly in the oral cavity are commonly referred to as orodispersible wafers according to the European Medicines Agency (EMA), medicated wafers that readily dissolve in the oral cavity are commonly referred to as orodispersible wafers or simply soluble films according to the FDA [7] [8]. Usually, fast-dissolving oral wafers are ultra-thin film (50-150 μm) with postage stamp size which dissolves in the oral cavity after contact with the saliva within a minute, resulting in rapid absorption and imminent bioavailability of the drugs [9]. Drugs loaded in buccal adhesive wafers are absorbed directly through the buccal mucosa, which after their absorption, delivers the drug to the systemic circulation [10]. Similarly, a wafer is frequently referred to as a paper-thin polymer film used as a pharmaceutical agent carrier. This innovative form of dosage is done by mouth but does not require water to absorb a drug [11].

1.1 Special features of medicated wafers [6] [12]

Medicated wafers boast several unique features that make them an attractive option for drug delivery. Characterized by their thin and elegant design, they offer ease of handling and consumption. Additionally, their availability in various sizes and shapes provides flexibility in dosage and administration. Notably, medicated wafers exhibit rapid disintegration upon contact with saliva, ensuring swift release of the drug. They are particularly suitable for delivering low-dose drugs, with effective delivery possible for doses up to 40 mg. Preference is often given to medicines with smaller to moderate molecular weights. Furthermore, the medication incorporated into these wafers should demonstrate excellent stability and solubility, both in water and saliva, ensuring consistent efficacy. Ideal candidates for medicated wafers are drugs that are partially unionized at the pH of the oral cavity, facilitating absorption and

bioavailability. These special features collectively contribute to the appeal and effectiveness of medicated wafers as a versatile and efficient drug delivery system.

1.2 Advantages over other oral dosage forms [3] [7] [13]

The various advantages of Orodispersible wafers over other oral dosage forms are fast dissolution, more stable, and resistance when compared to some Orodispersible tablets (ODTs), which are fragile and brittle. Oral wafers tend to be flexible and portable, while ODTs require a special transportation package. On the other hand, forms of liquid dosage are considered very flexible and an alternative to overcoming swallowing problems, but they are usually associated with certain limitations [7] [14]. Generally, the caregiver should be accurately uniform in liquids and carefully agitated before administration. The amount of volume is also an important consideration since small amounts may lead to inaccurate measures whereas large amounts may contribute to degrading the adherence of the patients. On the contrary, oral wafers allow improved dosing accuracy once each strip is produced to contain an accurate amount of the drug. In addition, elevated dose flexibility can also be achieved depending on the packaged device as an electronic tape dispenser can be used which enables individual strips to be dispensed with adjustable doses merely by controlling an electronic display system [15]. As previously referred, oral films are an easy portable dosage form in contrast to the large liquid bottles and measuring inconvenient devices to transport. In addition, it is also important to consider the poor stability of the liquid formulations, particularly the aqueous-based mixtures which, unlike most oral wafer formulations, require the addition of several substances to extend their shelf-life [16].

1.3 Why medicated wafers? Features for patients and companies [17]

Drug therapy and the intended patient group are the two most important factors to consider when developing an oral formulation. Choosing the type of pharmaceutical dosage form can be challenging when the target populations include very young children (birth to 8-10 years old) and the elderly. Developing a specific dosage for children of various ages is the primary concern of the pediatric section. Another consideration for both demographics is the potential difficulty of ingesting the larger dosage forms. Multiple nerves and muscles work in tandem to complete the swallowing motion. The ability to swallow safely is thought to be achieved by the time a child reaches the age of twelve. The swallowing function generally underlies an aging process, so some malfunctions may be associated with age, generally referred to as presbyphagia, but may also be caused by pathological circumstances, generally referred to as dysphasia [18]. There was a huge surge of interest in developing patient-centered formulations because of the strong correlation between these factors and patients' adherence to medication therapy. Orally dissolving dose forms, such as liquids, were thus the most popular and widely used with these demographics. As a result, oral wafers became a viable alternative to traditional oral dosage forms, making them more suitable and easy for people with swallowing issues [19].

2. Formulation Consideration

2.1. Active pharmaceutical ingredient

Various classes of drugs, including antiulcer medications like Omeprazole, antiasthmatics such as Salbutamol sulphate, antitussives, expectorants, antihistamines, and NSAIDs like Paracetamol and Tenoxicam, can be formulated as medicated wafers designed to dissolve in the mouth. The ideal characteristics of drugs suitable for incorporation into medicated wafers include pleasant flavoring and

low dosages (up to 40 mg), as well as low to moderate molecular weight, good stability, and solubility in both water and saliva. Moreover, drugs that exhibit partial unionization in the oral cavity, along with the ability to permeate oral mucosal tissue, are preferred for wafer formulation. Additionally, the presence of wafer-forming polymers is essential for the successful development of these dosage forms [20-21].

2.2. Polymers

A variety of polymers A polymer matrix with different physicochemical and functional properties can make up medicated wafers. One can manage several features, such as mucoadhesiveness, disintegration time, drug loading capacity, mechanical strength, elasticity, and handling capabilities, by adjusting the kind or grade of polymers, etc. An important consideration when developing oral film matrices is the choice of polymer (or mixes of polymers), which may differ depending on the target product profile. Extensive research and testing have been conducted on hydrophilic polymers such as HPMC E-3 and K-3, Pullulan, Gelatin, Sodium alginate, Hydroxy propyl cellulose, Polyvinyl alcohol, Maltodextrin, Eudragit, and Polymerized rosin, a new wafer forming polymer. The medical and nutraceutical fields have shown a lot of interest in the usage of dissolvable wafers made of wafer forming polymers. The mechanical properties, great tongue sensation, and rapid disintegration are all thanks to the water-soluble polymers used to make the Wafers. Polymer wafer, strip, and film base molecular weight enhancement [19] [20] [22].

2.3. Plasticizer

Wafer mechanical properties might be impacted by the plasticizer. The mechanical properties, including elongation and tensile strength, of the wafers were improved by using plasticizers. Their concentration can have an effect on these traits. The most common plasticizers include glycerol, dibutylphthalate, polyethylene glycols, and many more [23].

2.4. Sweetening agent

These days, sweeteners are ubiquitous in both food and medicine. When it comes to children, sweetness is key when it comes to wafer compliance. Oral dissolving formulations rely on sweeteners, both natural and artificial, to make them more palatable. Dextrose, fructose, glucose, liquid glucose, maltose, and sucrose (cane or beet sugar) are the traditional sweeteners. Faster absorption of fructose flavor in the mouth occurs as compared to dextrose and sucrose. Warning: people with diabetes or who are on a strict diet should not consume large amounts of the natural sugars used in these recipes. It is for this reason that artificial sweeteners have grown in popularity in both food and medicine. The first generation of artificial sweeteners includes saccharin, cyclamate, and aspartame; the second generation includes acesulfame-K, sucralose, alitame, and neotame. Herbal sweetener Rebiana, made from the South American plant Stevia rebaudiana, is roughly 200-300 times sweeter than competing brands. In place of artificial sweeteners, the stevia plant is superior [24].

2.5. Saliva stimulating agent

These agents (2-6%w/w) increase the saliva production rate, aids in the faster disintegration of wafers. The most commonly used saliva stimulating agents are citric acid, malic acid, lactic acid, ascorbic acid, tartaric acid.

2.6. Flavouring agents

The addition of these substances can enhance the palatability and compliance of medicated wafers with patients. Citrus, apple, cherry, raspberry, oleoresins, peppermint, cinnamon, nutmeg, vanilla, cocoa, coffee, chocolate, and many more flavoring agents are utilized. How much flavoring agent to use is determined by the type and intensity of the taste..

3. Manufacturing Processes Overview: From the Conventional to the Innovative [10] [19 [25]

When making dental films, solvent casting and hot-melt extrusion are the two most used methods. Some breakthroughs and fresh approaches have surfaced in the last several years. Semisolid casting and solid-dispersion extrusion are two examples of these production technologies that have been utilized alone or in conjunction with one another [26]. One example of an innovative manufacturing method is printing or rolling [27]. The first step mostly involves making a pre-mix, adding the psychoactive component, and then running the resulting matrix through a metering roller. The printing process entails printing the active pharmaceutical ingredient onto oral wafer placebos using certain techniques [28].

3.1. Solvent casting method

Approach to insolvent casting Hydroxpropyl methyl cellulose (HPMC), carboxy methylcellulose (CMC), polyvinyl alcohol (PVA), and hydroxyl propyl cellulose (HPC) are water-soluble polymers; excipients and drugs are dissolved in solvents. After that, you blend the two solutions thoroughly, pour them into a petri dish, let them dry, and finally, shape them anyway you choose.

3.2. Solid dispersion extrusion

Solid dispersions are made by extruding the medication and any immiscible components together. After that, dies are used to form the solid dispersions into wafers.

3.3. Hot melt extrusion

The drug is first solid-state combined with appropriate carriers in the hot-melt extrusion process. The next step is to melt the mixture using the extruder that comes with internal heaters. Lastly, dies are used to mold the melt into wafers.

3.4. Rolling method

In this method, both drug solution and polymer solutions are mixed thoroughly and loaded into the roller. After drying the film obtained is cut into a suitable size and shape

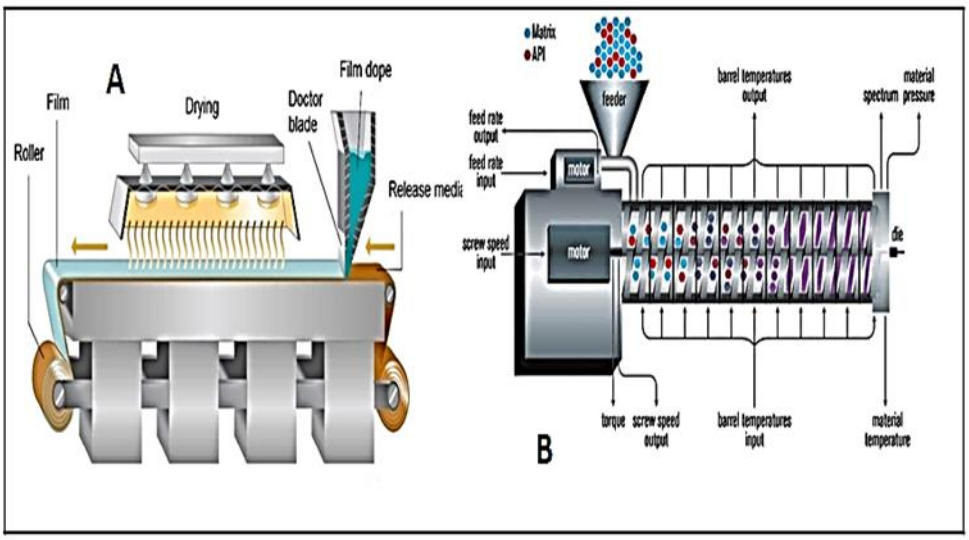

Fig.1: A Solvent casting method B) Hot melt extrusion

4. Characterization Methods [3] [29]

5. 4.1. Organoleptic evaluation

The oral wafers are designed to either disintegrate rapidly or remain in the oral cavity for extended periods, requiring the product to possess satisfactory

organoleptic qualities. The product must possess the necessary flavor and taste attributes that are appealing to a large demographic. Special human taste panels are closely watched to analyze the product's psychophysical characteristics. In-vitro methods for organoleptic assessments involve utilizing taste detectors and electronic tongue measurements to aid in taste masking and distinguish between different levels of sweetness.

4.2. Thickness

The wafer's thickness can be tested using a micrometer screw gauge at various key points. It is essential for assessing consistency in the wafer's density since it directly affects the accuracy of the wafer's dose.

4.3. Tensile strength

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by the applied load at rupture divided by the cross-sectional area of the strip as given in the equation below

$$\textbf{Tensile strength} = \frac{\text{Load at failure}}{\text{Wafer thickness} \times \text{wafer width}} \times 100$$

4.4. Percent elongation

When stress is applied, a strip sample stretches and this is referred to as a strain. Strain is the deformation of a strip divided by the original dimension of the sample. Generally, elongation of strip increases as the plasticizer content increases [30].

$$\%\ \textbf{Elongation} = \frac{\text{Increase in length of wafer}}{\text{Initial length of wafer}} \times 100$$

4.5. Tear resistance

The tear resistance of plastic film or sheeting is intricately linked to its ability to withstand rupture. The test is conducted at a low loading rate of 51 mm/min to measure the tearing force. The rip-resistance value is the maximal stress or force needed to tear the specimen, typically located around the beginning of tearing, and is measured in Newtons (or pounds-force).

4.6. Young's modulus

Young's modulus or elastic modulus is the measure of the stiffness of strip. It is represented as the ratio of applied stress overstrain in the region of elastic deformation as follows: [31]

$$\textbf{Young's modulus} = \frac{\text{Slope}}{\text{Strip thickness} \times \text{cross} - \text{head speed}} \times 100$$

Hard and brittle wafer demonstrate a high tensile strength and Young's modulus with small elongation.

4.7. Folding endurance

Folding endurance is determined by repeated wafer folding at the same location until the wafer breaks. The number of times the wafer is folded without breaking is calculated as the folding endurance value.

4.8. Disintegration time

The disintegration time requirement of 30 seconds or less for orally disintegrating tablets as stated in the CDER instruction can be applied to fast-dissolving oral wafers. Although there is no official protocol available for oral quickly dissolving wafers, they can serve as a qualitative reference for quality control testing or during the development process. For this investigation, Pharmacopoeial disintegrating test devices may be used. The usual duration for wafer disintegration ranges from 5 to 30 seconds. Research on wafer swelling is conducted using a simulated saliva solution [32].

4.9. Swelling property

Wafer swelling study is conducted using simulated saliva solution. The wafer sample is weighed and put in a plastic container in a wire mesh of stainless steel

comprising a 15mL medium. Increase in wafer weight is determined at a predetermined time interval until the observation of a constant weight. The swelling degree is calculated using formula

$$\alpha = \frac{(Wt - Wo)}{Wo}$$

Wt is the weight of Wafers at time t, and WO is the weight of Wafers at time zero

4.10. Taste evaluation

A taste panel of six human volunteers evaluated the taste acceptability of a 10 mg medicine by placing a wafer sample containing the drug in their mouths until it disintegrated, then spitting it out and recording the flavor. The volunteers were asked to gargle with distilled water between the medication and sample administration. Following scale was Used for the indicating taste-masking values: + = very bitter, ++ = moderate to bitter, +++ = somewhat bitter, ++++ = tasteless/taste-masked.

4.11. Transparency

A UV spectrophotometer can be used to measure the transparency of the wafers directly. Cut the wafer samples into rectangles and lay them on the spectrophotometer cell's inner surface. Calculate the transmission of wafers at a wavelength of 600 nm.

Transparency = (logT600)/b = - €c

Where T600 is the transmittance at 600 nm, b is the Wafer thickness (mm), c is the concentration

4.12. Hydration capacity

The hydration capacity (HC) of the wafers is performed by incubating them at 37±0.1^{0}C in 25mL of Phosphate buffer solution (PBS pH 6.8). The wafers (n¼4) were initially weighed and the swelling behaviour was observed at predetermined time intervals. The samples have been separated, closely blotted out between tissue documents to remove liquid droplets adhered to the surface, and reweighed to constant weight. The proportion of water consumption was calculated as follows.

$$\textbf{Water uptake } \% = \frac{(Ws - W)}{W} \times 100$$

Where Ws is the weight of the hydrated wafer and W is the initial weight of the wafer [31] [33].

4.13. *In-vitro* Dissolution Test

The traditional basket or paddle apparatus specified in the pharmacopoeia can be utilized for conducting dissolution testing. The dissolution medium will be selected based on the sink conditions and the highest API dose. The wafer's tendency to float on the dissolving liquid when the paddle system is utilized can make the dissolution test challenging.

4.14. Stability test

A piece of wafer preparation was stored in an aluminium package at 25^0 C with 50-60% humidity (normal condition) or at 40 with 75% humidity (accelerated condition) for 4-24.

4.15. Assay/ Content uniformity

Determine this using any standard assay method specified in the pharmacopoeia for the particular active pharmaceutical ingredient. Content homogeneity is assessed by measuring the API content in a single strip. The content uniformity limit ranges from 85% to 115%.

5. Advanced Oral Medical Wafers [34]

It offers medication in a flat, film, or wafer form for use in the mouth. Initially, it may seem akin to conventional oral tablets, but it differs significantly. Traditional systems use the mouth as a pathway to deliver medication into the gastrointestinal tract. A flash release wafer in its simplest form produces the same effect. Oral wafer pharmaceutical systems utilize the mouth for both application and drug action [25] [26] [35]. The size of this dosage form can range from 2cm² to 8cm² in area and from 20µm to 500µm in thickness. The amount of medicine in each oral medical wafer is determined by the drug's physicochemical qualities. Oral wafer medication is administered in the oral cavity, including the tongue, gingiva, teeth, buccal area, or upper palate, and is

absorbed there. It offers both systemic and local effects.

Three distinct oral wafer medicine systems cater to the specific needs of patients. Various types of oral medical wafers can provide distinct pharmacokinetic profiles and prevent adverse effects in the gastrointestinal tract [27].

6. Rationale Behind use of Medicated Wafers [2] [37]

A medicated wafer reduces drug toxicity and adverse reactions by regulating drug and metabolite levels in the blood at specific sites. It allows for lower drug doses to achieve the same therapeutic effect as higher doses through controlled release. This targeted drug delivery system ensures drugs are released locally where needed, minimizing adverse effects. By delivering a consistent blood concentration and predictable drug distribution, it optimizes treatment outcomes. The oral mucosa is an ideal site for administering many active ingredients due to its direct access to the bloodstream and high patient compliance.

7. Patented Approaches

7.1. X Gel

XGelTM is a GMO wafer that provides unique benefits to healthcare and pharmaceutical industries. It is derived from non-animal sources, meets religious guidelines, and is suitable for vegetarians. XGelTM wafer systems can encapsulate several types of oral dosage forms and are soluble in either cold or hot water. The product comprises a range of water-soluble polymers tailored for the intended application. [11, 37-38].

7.2. Soluleaves^{TM}

This method is utilized to produce a range of oral administration wafers that can contain active substances, colors, and flavors. SoluleavesTM wafers are designed to rapidly disintegrate upon contact with saliva, releasing the active ingredients and tastes promptly. Edible wafers are an excellent delivery strategy for goods that need to be quickly released in the mouth due to their quality. This approach is found to be particularly suitable for children or elderly people who may have difficulty swallowing conventional tablets or capsules. The delivery mechanism is applicable for treating cough, cold, gastrointestinal issues, discomfort, and dietary goods. The wafers can be designed to stick to mucous membranes and gradually release the active substance over a 15-minute period.

6.3. Wafertab

WafertabTM is a medicine delivery device that combines pharmaceutical active components onto a consumable wafer strip. Upon contact with saliva in the mouth, the strip rapidly dissolves and releases active chemicals. This wafer strip is sweetened to help improve taste masking. The WafertabTM scheme offers numerous potential for inventive product design by enabling the bonding of different films with unique characteristics. It comes in various forms and sizes and is an ideal method for administering medications that need to be quickly released or for individuals who have trouble swallowing.

7.4. Foamburst

This is a distinctive iteration of the SoluleavesTM technology in which an inert gas is introduced into the wafer during the production process. This results in a wafer with a honeycomb structure that dissolves rapidly, creating a unique sensation in the tongue. FoamburstTM has attracted the attention of food and garment makers as a method for transferring and releasing flavors.

8. Clinical and Regulatory Aspects [39]

If the product is found to be bioequivalent to the present oral version of the same medicine, the US Food and medicine Administration (USFDA) requires following the Abbreviated New Drug Application (ANDA) procedure. No clinical

investigations have been conducted about this generic approval method outlined in section 505(j) of the Food, Drug, and Cosmetic Act. An instance of this scenario could be comparing the bioequivalence of an orally disintegrating tablet (ODT) with an orally disintegrating film (ODF). The oral film product generated may exhibit unique pharmacokinetic profiles in comparison to the existing product. The ODF is categorized as a new dosage form and must adhere to the approval processes outlined in section 505(b) (2). A new clinical investigation is required in this scenario. The new clinical study offers the advantage of granting the product 3 years of exclusive marketing rights. Preclinical toxicity studies are not necessary if the chemical matches the approved product. These studies aim to demonstrate solely the security, tolerability, and effectiveness aspects. Oral mucosal irritation testing is conducted in both animal and human models. Marketing authorization permission is essential in Europe according to the regulations of the European Medicine Evaluation Agency. You can choose between two methods: decentralization or mutual recognition [40] [41].

9. Packaging of Thin Wafers [3] [38] [42]

It is essential in the pharmaceutical sector for the selected packaging to preserve the integrity of the product. Various packaging options are available for oral fast-dissolving wafers. Individual packing for wafers is mandatory. The most commonly utilized packaging format is an aluminum pouch. Oral thin wafers are packaged using various materials such as foil paper, plastic bags, single bags, aluminum bags, multi-unit blister packaging, and barrier film. Barrier films are commonly utilized for pharmaceuticals that are very sensitive to moisture.

Table 1: List of polymers used in medicated wafer formulations

Property	Pectin	Carboxy methyl cellulose	Hydroxy propyl methyl cellulose	Pullulan	Gelatin
Synonym	Methopectin, Citrus pectin, Pectinic acid	CMC sodium, Akulell, Blanose, Aquasorb,	HPMC, Methocel, Metolose, Benecel	Pullulane, 1, 6 α linked maltotriose	Byco, cryogel, Instagel, Solugel
Description	It occurs as yellowish white, odourless powder with mucilaginous taste	It is white odourless powder	Odourless, tasteless and white or creamy white fibrous or granular powder.	It is available as white, odourless tasteless, stable powder	It occurs as light amber to faintly yellow colored, vitreous, brittle solid. It is odorless, tasteless.
Film forming capacity	It has a film forming ability	It has a good film forming ability	It has a film forming ability in 2–20%w/w concentrations.	5–25%w/w solution forms flexible films. Films are low permeable to oxygen, stable	It has a very good film forming ability.

Application	Pectin is used for the continuous release of drugs as a gel forming agent. It was used for the shipment of colon drugs in conjunction with other polymers.	It is commonly used in oral and topical wording. It is primarily used as an agent that increases viscosity. It is used to prepare suspensions and emulsions as a stabilizer. Depending on the grade and concentration used in the formulation, it can be used as a binder or disintegrant.	In oral, ophthalmic and topical formulations, hypromellose is commonly used. Hypromellose is mainly used as a tablet binder, film coating agent, film forming agent, and as an extensive release formulation matrix.	It is widely used to provide bulk and texture in the food industry. Pullulan's hydrophobic grades are used to make nanoparticles ready for targeted delivery. As a plasma expander, pullulan can be used as a substitute for dextran	It is widely used in an implantable delivery system. It is used for the preparation of hard and soft gelatin capsule. It is used for microencapsulation of drugs. It is used topically in wound dressing

10. Marketed Formulations of Wafers [3] [6] [43]

The pharmaceutical industry has seen a growing demand for innovative drug delivery systems that enhance patient compliance, particularly in populations like children and the elderly. Among these, fast-dissolving wafers, strips, or films have gained significant attention due to their ease of administration, rapid onset of action, and convenience. These formulations dissolve quickly upon contact with saliva, eliminating the need for water or swallowing, which is particularly beneficial for patients with dysphagia or those requiring immediate relief. Several marketed products exemplify the versatility of this dosage form, catering to a wide range of therapeutic applications. Table 2 highlights some of these formulations, showcasing their active pharmaceutical ingredients (APIs), manufacturers, and intended uses. For instance, products like Listerine (Cool Mint) by Pfizer offer relief from mouth ulcers, while Klonopin wafers containing Clonazepam by Solvay Pharmaceuticals address anxiety disorders. These innovations not only improve drug delivery but also enhance patient satisfaction and adherence to treatment regimens.

Table 2: List of some marketed products available as fast dissolving wafers/ strips/ films

Product	**API**	**Manufacture**	**Use**
Listerine	Cool mint	Pfizer, Inc	Mouth ulcer
Benadryl	Diphenyhydramine HCL	Pfizer	Antiallergic
Suppress	Menthol	InnoZen, Inc	Cough suppressant

Klonopin wafers	Clonazepam	Solvay pharmaceuticals	Antianxiety
Theraflu	Dextomeyhorphan	Novartis	Antiallergic
Orajel	Menthol/Pectin	Del	Mouth freshener
Gas-X	Simethicone	Novartis	Antiflatuating
Chloraseptic	Benzocain/menthol	Prestige	Sore throat

11. Patent Registered on Wafers/Oral Film [11] [37] [38] [44]

Table 3: Recent patents on fast dissolving strips/wafers/films

Sr. No	Title	Patent no	Inventor	Issued	Assignee
1	Water soluble film for oral administration with instant wettability	US5948430A	Zerbe et al	Sept 7, 1999	LTS Loman Therapie-system GmbH
2	Bioderodable films for delivery of pharmaceutical compounds to mucosal surface	US6159498A	Tapoisky et al	Dec 12, 2000	-
3	Fast dissolving orally consumable films containing sweetners	US2003/0211136A1	Lori et al	Nov 13, 2003	Warner Lambert company LLC
4	Fast dissolving film for oral administration of drug	US2004/0208931A1	Friend et al	Oct 9, 2004	William Squire, Esq.
	Fast dissolving consumable films containing modified starch for improved heat and moisture resistance	US2004/0247648	David et al	Dec 9, 2004	Warner Lambert company LLC
6	Fast dissolving orally consumable films	US7025983B2	Leung et al	April 11, 2006	-
7	Dissolving thin film xanthone supplement	US7182964B2	Kupper et al	Feb 27, 2007	-
8	Thin film strips	US7241411B2	Berry et al	Jul 10, 2007	Acupac packaging. Inc
9	Disintegrable film for diagnostic devices	US7470397B2	Meathrel et al	Dec 30, 2008	

10	Pharmaceutical carrier devices suitable for delivery of pharmaceutical compounds to mucosal surface	US7579019B2	Tapoisky et al	Aug 25, 2009	Adhesive research. Inc
11	Film comprising nitro-glycerine	US20100215774A1	Maibach and Todd	Aug 26, 2010	-
12	Dissolvable tobacco film strips and method of making the same	US7946296B2	Wern et al	May 24, 2011	-

12. Applications

Medicated wafers have demonstrated wide-ranging applications, particularly in therapies requiring rapid drug absorption, such as those used to manage pain, allergies, sleep disorders, and central nervous system disorders. These wafers offer versatility in delivery methods, with potential applications including: In topical applications, dissolvable wafers show promise for delivering active agents such as antimicrobial or analgesic agents in wound care and other therapeutic settings, offering a convenient and mess-free alternative..For vaginal drug delivery, specially designed wafers offer a manual administration method without the need for gel or cream applicators, reducing inconvenience. Upon contact with vaginal fluid, the components of these wafers hydrate to form a hydrogel, providing effective delivery of medications without the associated mess. In gastrointestinal delivery systems, dissolvable wafers are utilized in dosage forms containing both water-soluble and poorly soluble molecules in film format. Wafer dissolution can be triggered by gastrointestinal tract (GIT) pH or enzyme secretion, making them suitable for the treatment of gastrointestinal disorders. This versatility highlights the potential of medicated wafers in various therapeutic contexts, offering innovative solutions for drug delivery challenges [45].

13. Challenges in Formulation Development

Nowadays, oral wafers are an alternative in the market due to the patient's preference for tablets and capsules. Oral thin wafer technology is still in the beginning stages and will be the first preference of patients in the future. Since 2003, North America is having more than 80 oral thin film brands, but, the market remained limited when compared to oral dissolving tablets. In the US market, the OTC wafers/films for pain management and motion sickness are commercialized. Now, the prescription of oral films has been approved in three major countries, i.e. US, EU, and Japan. These approved films have the potential to dominate over other dosage forms of the same drugs. It seems that the value of the oral film market will grow significantly. Today, huge literature is available for formulation development and evaluation of oral fast dissolving or fast disintegrating tablets and wafers. However, formulator comes across some challenges while the development of such dosage forms. There is a need to address such challenges which may help in the future to explore the area in research and that may help in overall formulation and development. These challenges are directly related to patient compliance. Hence, preference should be given to them in formulation development. Following are some of the challenges in formulating fast dissolving oral wafers and trying to elaborate and solve these problems [47-48].

13. Future Prospective

Nowadays, enormous advancements have been made in oral drug delivery technologies by the pharmaceutical industry. The market has moved a long way from conventional tablets/capsules to modern-day fast disintegrating and rapidly acting tablets/films and wafer formulations. A range of limitations such as lower bioavailability of oral solid drugs, inaccurate dosing by liquid formulations, the difficulty of administering injections, etc are keystone which has turned the focus of pharmaceutical industries to develop novel oral dosage forms that eliminate these limitations [49] [50].

The ODF is classified as the "new dosage form" and the approval processes of section 505(b) (2) must be followed. A fresh clinical study would be needed in this situation. The benefit of the fresh clinical study is that the item would be awarded 3 years of exclusive marketing. Preclinical toxicity studies are not required if the molecule is the same as that of the approved product. Safety, tolerability, and efficacy features are to be demonstrated in such trials. Oral mucosa-irritation testing is carried out in both animal models and humans. The future looks very promising for the film and wafer technology in the time to come as new technologies are rapidly introduced to prepare thin films as well as wafers [51] [52].

Conclusion

Many of the pharmaceutical companies are turning their product franchise from ODTs to ODF also known as ODWs or in the form of medicated wafers as a consumer-friendly option. This technology choice can also provide a useful platform for the growth of the patent-free product. ODWs enable product brand extension. The OST is a useful instrument for managing the product life cycle to improve the patent life of current molecules or products. The ODWs are comparatively simple to produce compared to some of the complex and costly processes (such as lyophilization) used to produce ODTs; thus, lowering the general treatment cost. Not only has the implementation of ODWs / ODF been restricted to a buccal rapid dissolving scheme, but it also extends its horizon to other apps such as gastroretentive, dental, topical, implantable, sublingual delivery. This distribution platform demonstrates potential company promise in pharmaceutical, nutraceutical, and cosmeceuticals products for the future. The OST is a useful instrument for managing the product life cycle to improve the patent life of current molecules or products.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Authorship contribution statement

Swapnil Chopade, Popat Kumbhar: Supervision, Validation, Methodology, **Esther Gaikwad**: Investigation, Writing – original draft, **Sayali Powar:** Conceptualization, Administration **Tejaswini Burse:** Funding, Data Curation.

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