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CURRENT REVIEW ON FAST DISSOLVING ORAL WAFERS

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ABSTRACT

The difficulty of creating a dose form to enhance patient persuasion and compliance with a certain drug delivery method has increased. The other dosage form is the most agreeable and pleasant due to the wafer's thinness and tiny size. For paediatric and elderly patients, the introduction of oral wafers as the medication delivery mechanism offers an alternative to tablets, capsules, and liquid oral dose forms. Recently the Fast-Dissolving Film or Wafer are gaining the interest as alternative to the fast-dissolving tablets which definitely eliminates the fear of patients of chocking. Wafers are better than other traditional dose forms and other oral solid dosage forms that disintegrate in the mouth. The selection of medications to be included is the main challenge in wafer formulation. To increase patient compliance, wafers with a modest dosage of the active pharmaceutical ingredient (API) and a pleasant mouthfeel are created. The wafers need to be packaged carefully and handled with care when being stored, transported, and handled. Wafers have gained popularity among the elderly and paediatric populations despite these challenges due of their simplicity of administration and bioavailability.

Keywords: Oral wafers, Fast dissolving dosage forms, Oral administration, Bioavailability Enhancement.

INTRODUCTION

In the recent years, many of the pharmaceutical groups are focusing their research on rapid dissolving technology. This technology evolved over the past few years from the confection and oral care markets in the form of breath strips and became a novel and widely accepted form by consumers, so fast dissolving oral wafer are gaining the interest of large number of pharmaceutical industries. The main advantage of this technology is the administration to pediatric and geriatric patient population where the difficulty of swallowing larger oral dosage forms is eliminated. This fast dissolving drug delivery system (FDDS) is suited for the drugs which undergo high first pass metabolism and is used for improving bioavailability with reducing dosing frequency to mouth plasma peak levels, which in turn minimize adverse/side effects and also make it cost effective. Orally fast dissolving wafers is the type of drug delivery system which when placed in the oral cavity, disintegrate or dissolve within few seconds without the intake of water. Fast dissolving oral wafers are very similar to postage stamp in their shape, size and thickness. The present review provides an account of various formulation considerations, method of preparation and quality control of the fast-dissolving oral wafers[1-2].

To eliminate the drawbacks of fast dissolving tablet a fast-dissolving wafers can be placed. Fast dissolving wafers are very similar to ultra-thin strip of postage stamp in their shape, size and thickness. Fast dissolving wafers are formulated using polymers, active pharmaceutical ingredients (API), plasticizers, saliva stimulating agents, sweeteners, flavors, preservatives and colors. Fast dissolving wafers is simply placed on the patient's tongue or any oral mucosal tissue, instantly wet by saliva the wafers rapidly hydrates and adheres onto the site of application. It then rapidly disintegrates and dissolves to release the medication for oromucosal absorption or with formula modifications, will maintain the quick-dissolving aspects allow for gastrointestinal absorption to be achieved when swallowed. Technology Catalysts forecasts the market for drug products in oral thin wafers formulations to be valued at $500million in 2007 and could reach $2 billion. More importantly, prescriptions of fast dissolving wafers have been now approved in US, EU and Japan which are the three major regions. These approved wafers, have potential to dominate over other oral dosage forms of the same drugs. It seems that the value of the overall oral thin wafers market will grow significant[3-4].

Oral wafers

Oral wafers/oro-dispersible wafer strips These are paper thin polymer films of typically 2-8 cm2 area and 20- 500 µm thickness, containing typically less than 50 mg of API. They are administered directly on the tongue[5].

Benefits

- Increasing the bioavailability of the oral administered drugs that otherwise undergo hepatic first-pass metabolism
- It improved the patient compliance due to the elimination of pain with injections.
- Drug absorption can be terminated in case of the emergency.
- It offers passive system, which does not require any activation process. Salient Features
- Thin elegant film
- Available in various size and shapes
- Excellent mucoadhesion
- Fast disintegration
- Quick dissolution
- Rapid release
- Adaptable and amenable to existing processing and packaging machinery

- Cost effective[6].

Anatomic and Physiological Considerations while preparing wafers:

Physicochemical properties of the oral mucosa:

The surface of buccal cavity comprises of stratified squamous epithelium which is essentially 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 called membrane coating granules present at the uppermost 200 micron layer[7-8].

Anatomical features of oral cavity

The oral cavity is surrounded by the lips and is composed of two separate regions, the vestibule, the area between the cheeks, teeth, and lips, and the oral cavity proper. The oral cavity proper is mostly filled with the tongue and bounded anteriorly and on the sides by the alveolar processes containing the teeth and posteriorly by the isthmus of the fauces. Anteriorly, the roof forms by the hard palate and posteriorly by the soft palate. The uvula hangs downwards from the soft palate. The mylohyoid muscles constitute the floor of the oral cavity proper. A mucous membrane known as the oral mucosa is composed of stratified squamous epithelium and forms the inner lining of the mouth. Several submandibular and sublingual salivary glands secrete viscous and mucoid fluid to lubricate and keep the oral cavity moist[9-10].

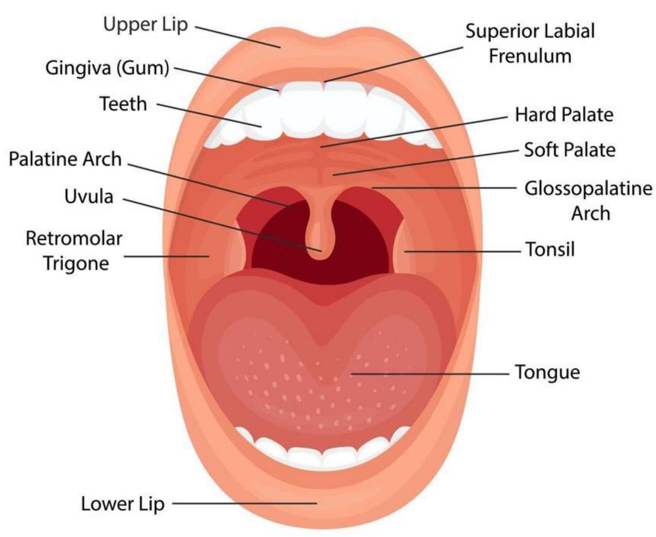

Figure 1: Anatomy of oral cavity

Mechanism of action of wafers

Wafers are placed on a patient's tongue or any oral mucosal tissue. They are instantly wet by saliva due to the presence of hydrophilic polymer and other excipients; the film rapidly hydrates and dissolves to release the medication for mucosal absorption[11].

Classification of oral wafers

Flash release wafers

- Area–2-8 cm2.
- Thickness–20-70 µm.
- Dissolution–60 s maximum.
- Single layered structure.
- Soluble excipients are used.
- Highly hydrophilic polymers are required.
- Drugs are dispersed in solid solution phase.
- It is applied to the upper palate of the tongue.

Mucoadhesive melt-away wafers

- Area–2-7 cm2.
- Thickness–50-500 µm.
- Dissolution–1-3 min.
- Single or multi-layered structure
- Soluble excipients are used.
- Hydrophilic polymers are required.
- Drugs are dispersed in solid solution or suspension.
- It is applied to gingival or buccal region.

Mucoadhesive sustained release wafers

- Area–2-4 cm2.
- Thickness–50-250 µm.
- Dissolution–8-10 h[12-13].

Ingredients used for forming oral wafers

Water soluble polymers:

Water-soluble polymers are used as Wafer formers. The use of Wafer forming polymers in dissolvable wafers/films has attracted considerable attention in medical and nutraceutical application. The water-soluble polymers achieve rapid disintegration, good mouth feel and mechanical properties to the Wafers[14].

Drugs:

Different classes of drugs can be formulated as mouth dissolving Wafers including Antiulcer (e.g. Omeprazole), Antiasthamatics (Salbutamol sulphate), Antitussives, Expectorants, Antihistaminics, NSAID'S (e.g. Paracetamol, Meloxicam)[15].

Penetration enhancers:

Penetration enhancers are also required when a drug has to reach the systemic circulation to exert its action. These must be non-irritant and have a reversible effect: the epithelium should recover its barrier properties after the drug has been absorbed. The most common classes of buccal penetration enhancers include fatty acids, surfactants and, among these, bile salts, azone and alcohols[16].

Surfactants:

Surfactants are used as solubilizing or wetting or dispersing agent so that the Wafer is getting dissolved within seconds and release active agent immediately. Some of the commonly used are Sodium Lauryl Sulfate, Benzalkonium chloride, Bezthonium chloride, Tweens etc [17].

Sweetening agents:

Sweeteners have become the important part of the food products as well as pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. Sweetness plays important role for improving compliance wafers in paediatric population. Natural sweeteners and artificial sweeteners, plays vital role to improve the palatability of the oral dissolving formulations. The classical source of sweetener is sucrose (derived from cane or beet in the form of liquid or dry state), dextrose, fructose, glucose, liquid glucose and maltose[18].

Taste Masking Agents:

Taste masking of bitter or objectionable tasting drug substances is critical for any orally administered dosage form. There are various approaches of taste masking of bitter drugs for fast dissolving dosage forms, Polymer coating to the Solution of drug or its suspension applied to a substrate, Particles or entities of active drug are coated directly[19].

Colour:

A full range of colours is available, including FD & C colours, EU Colours, Natural Colours and custom Pantone-matched colours[20].

Saliva stimulating agents:

Saliva stimulating agents Increases the saliva production rate, aids in faster disintegration of wafers (Conc. - 2-6 % w/w). Examples citric acid, malic acid, lactic acid, ascorbic acid, tartaric acid Flavouring agents: may be selected from syn. Flavour oils, oleoresins, from plant parts. Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid are the few examples of salivary stimulants, citric acid being the most preferred amongst them[21-22].

Flavor:

Any flavor can be added, such as intense mints, sour fruit flavors or sweet confectionery flavors. Flavoring agents Perception for the flavors changes from individual to individual depending upon the ethnicity and liking. It was observed that age plays a significant role in the taste fondness. Flavouring agents can be selected from synthetic flavour oils, oleo resins, extract derived from various parts of the plants like leaves, fruits and flowers. Flavours can be used alone or in the combination. Peppermint oil, cinnamon oil, spearmint oil, oil of nutmeg is examples of flavour oils while vanilla, cocoa, coffee and chocolate[23].

MANUFACTURING METHODOLOGIES OF WAFER

Rolling method

A solution or suspension containing drug is rolled on a carrier. The solvent is mainly water or a mixture of water and alcohol. The wafer is dried on the rollers and cut into desired shapes and sizes. Other ingredients including active agents dissolved in a small portion of aqueous solvent using the high-shear processor. Water soluble hydrocolloids are dissolved in water to form homogeneous viscous solution [24-25].

Hot-melt extrusion

The active moiety and other ingredients are mixed in a dry state, subjected to the heating process and then extruded out in a molten state. The solvent is completely eliminated. The strips are further cooled and cut to the desired sixe. The high temperature used in this process may degrade thermolabile APIs [26-28].

Table 1: Advantage and Disadvantages of Hot-melt extrusion

Advantages	Disadvantages
▪ Compressibility properties of the API may not be of importance. ▪ Good dispersion mechanism & bioavailability for poorly soluble drugs. ▪ No need to use solvent or water. ▪ Fewer processing steps. ▪ More uniform dispersion of the fine particles because of less intense mixing and agitation. ▪ Less energy compared with high shear methods. ▪ Cost effective process with less processed time and unit operations	▪ Flow properties of the polymers are essential to processing ▪ Thermal degradation due to high temperature. ▪ Lower melting point binder risks a situation where melting/softening of the binder occurs during handling and storage of agglomerates. ▪ Higher melting point binders require high melting temperature and can contribute to volatility problems especially for heat labile materials.

Solvent Casting Method

This technique is employed to manufacture fast dissolving wafers of size 3x2 cm2 and 2x2 cm2. Water soluble polymers are dissolved in the aqueous vehicle. The drug along with other excipients is dissolved in suitable solvent, and both are mixed and stirred. It is finally casted on Petri dish or plate made up of glass, plastic or Teflon and dried. Specific types of equipment are used at large scale production as well as rollers are used for pouring the solution on an inert base. Entrapped air is removed by vacuum. The final step is drying the wafer, removes the solvent and helps to obtain the finished product. Wafers are dried after which cutting, stripping and packaging is done[29-30].

Table 2: Advantage and Disadvantages of Solvent Casting Method

Advantages	Disadvantages
▪ Better uniformity of thickness and better clarity than extrusion. ▪ Wafer has fine gloss and freedom from defects such as die lines. ▪ Wafer has more flexibility and better physical properties.	▪ The polymer used must be soluble in volatile solvent or water. ▪ Stable solution with a reasonable minimum solid content and viscosity should be formed.

	▪ Multiple casting techniques may be selected on the basis of the fluid rheology, desired applied mass and required dosage uniformity. ▪ Formation of a homogeneous and release from the casting support must be possible

Freeze-dried wafers

A polymer of concentration 1% (w/w) and lactose as a bulking agent of concentration 6% (w/w) was added to deionized water and mixed for 45 min. 1.5 ml of the various polymer solutions was pipette out into the cylinder cavities pre-oiled with mineral oil. The formulation was subjected to a freeze-phase in a freeze-dryer at-60°C for 2h & the dying phase was executed at a pressure of 25 m-tor for 24 h. Wafers were stored in glass jars with 2g of desiccant sachets [31-32].

Solid dispersion extrusion

The immiscible components are extruded with drug, and then solid dispersions are prepared. Solid dispersions are shaped in wafers by use of dies[33].

Advantages

• More uniform dispersion of the fine particles because of intense mixing and agitation

• Fewer processing steps.

Evaluation of wafers

Color: It should be attractive and good patient compliance.

Weight: The wafer were subjected to mass variation study by individually weighing randomly selected patches. The average of 5 observations of each batch was calculated. Same done for each batch.

Appearance, Size and Shape: The formulated wafer were checked for their appearance, shape and thickness. The thickness of the wafer was determined at two different places using a digimatic micrometer and mean value was calculated[34].

Folding endurance:

To estimate the mechanical properties of a wafer. It is measured by repeatedly folding a wafer at the same point until it breaks. Folding endurance value is number of times the wafer is folded without breaking. Higher folding endurance value depicts the more mechanical strength of a wafer. As mechanical strength is governed by plasticizer concentration so it is clearly evident that plasticizer concentration also indirectly affects folding endurance value

Drug content uniformity / Assay:

Wafer dissolved in simulated saliva (100 ml pH 6.8) by homogenization for 30 min continue shaking. Content uniformity estimating the API content in individual wafer. Limit: 85-115% [35].

Disintegration time: Disintegrating time is defined as the time (seconds) at which a wafer breaks when brought in contact with water or saliva. Typical disintegration time for wafer is 5-30 seconds [36].

Dissolution time: The cumulative drug release and the cumulative percentage of the drug is calculated. Invitro drug dissolution is performed by using USP paddle type apparatus. The studies were carried out at 37°C of stirring speed 75 rpm in 900 ml phosphate buffer (pH 6.8). 5 ml of the samples withdrawn at the predetermined time intervals of 2, 4, 6, 8, 10 min and they are replaced within the same volume of buffer. The samples were collected and the concentration were determined at the appropriate wavelength by using UV-visible spectrophotometer [37].

% Moisture Uptake:

% Moisture Uptake Formulation was exposed to an atmosphere of 84% RH at28°C for three days using a saturated solution of NaCl. After three days the wafer was removed, weighed and percentage moisture absorbed was calculated. Average percentage moisture absorption of each wafer was calculated

Stability studies:

The purpose of the stability testing is to provide evidence on how the quality of the drug substance or the drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and the light, enabling the recommended storage condition, retest periods and the shelf life. The stability studies were carried out as per the International Conference of harmonization (ICH) Guidelines. The Stability studies were carried out at 40º C / 75% RH for 3 months. The optimized wafer formulations were packed in amber colored bottles, which were tightly plugged with cotton and capped. They are stored at 40ºC / 75% RH for 3 months and these are evaluated for their physical appearance, drug content and in-vitro dispersion time at specified intervals of time [38].

Diffusion study:

Before the diffusion study, drug assay and uniformity of OME within the wafer was determined. This is measured by weighing wafer accurately 5mg and hydrated in 8 mL of drug dissolution media. These hydrated wafer was stirred at the 37± 0.5°C until it completely get dissolved. The concentration of OME was analyzed by using UV Spectrophotometry.

Surface pH:

Done by placing the wafer on the surface of 1.5% w/v agar gel followed by placing pH paper (pH range 1-11) on wafer. The change in the colour of pH paper was observed and report.

Table -3: Some marketed oral wafers

Name of drug	Drug used for	Reference
Klonopin	Anticonvulsive and anxiolytic	(Troester *et al*., 2010)[39]
Tizanidine HCl	Skeletal muscle relaxant	(El-Mahrouk *et al*., 2014)[40]
Rizatriptan	Migraine	(Adelman *et al*., 2000) [41]
Sertaconazole	Candidiasis	(Hajhashemi *et al*., 2023)[42]
Loratadine	Hay fever, conjunctivitis	(Chakraborty *et al*., 2013) [43]
Temozolomide and Carmustine	Brain cancer	(Shapira-Furman *et al*., 2019) [44]
Gliadel	gliomas	(Gururangan *et al*., 2001)[45]
Benzydamine hydrochloride	Oral mucositis	(Mehravaran *et al*., 2022)[46]
Berberine	Oral Mucositis	(Vaezi *et al*., 2022)[47]
Ketorolac Tromethamine	Severe pain	(Mostafa *et al*., 2020)[48]
Carmustine	Brain tumours, non-Hodgkin's lymphoma and Hodgkin's lymphoma.	(Márquez-Rivas *et al*., 2010)[49]

CONCLUSION

Medicated Wafers as novel drug delivery systems having a better patient compliance and may offers to improve biopharmaceutical 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. In the recent trend of obtaining a palatable dosage form, wafers as an orodispersible film have made its own place & met in the expectation of the rising demand. Wafers are formulated as a advancement to oral fast dissolving films with its special properties of the high absorption and the high bioavailability. It is so popular among the people of all ages but particularly among geriatric and paediatric population because of is compatibility and the good mouth feel. The marketed products of the wafers are still less but there are so many more to come in the market.

REFERENCES

1. Garsuch V, Breitkreutz J. Novel analytical methods for the characterization of oral wafers. European Journal of Pharmaceutics and Biopharmaceutics. 2009 Sep 1;73(1):195-201.
2. Kelodiya J, Shah SK, Tyagi CK, Budholiya P. formulation, development of fast dissolving sublingual wafers of an antiemetic drug using film former. Journal of Pharmaceutical Education and Research. 2021;10(4):71-8.
3. Sushmitha S, Priyanka SR, Krishna LM, Murthy MS. Formulation and evaluation of mucoadhesive fast melt-away wafers using selected polymers. Research Journal of Pharmacy and Technology. 2014;7(2):176-80.
4. Dangi S, Kumar R, Goswami RB, Chaturvedi P. development of fast dissolving sublingual wafers of sitagliptin by film former.2021
5. Galey WR, Lonsdale HK, Nacht S. The in vitro permeability of skin and buccal mucosa to selected drugs and titrated water. J Invest Dermatol 1976;67:713-7.
6. Arunkanth. Novel drug delivery technologies: a challenging global scenario. Indian J Sci Technol 2013;8:468-82
7. Yakubov GE, Gibbins H, Proctor GB, Carpenter GH. Oral mucosa: Physiological and physicochemical aspects. Mucoadhesive materials and drug delivery systems. 2014 May 2:1-38.
8. Bartlett JA, van der Voort Maarschalk K. Understanding the oral mucosal absorption and resulting clinical pharmacokinetics of asenapine. Aaps pharmscitech. 2012 Dec;13:1110-5.
9. Johnston TP. Anatomy and physiology of the oral mucosa. Oral mucosal drug delivery and therapy. 2015:1-5.
10. Yousem DM, Chalian AA. Oral cavity and pharynx. Radiologic Clinics of North America. 1998 Sep 1;36(5):967-81.

11. Agarwal J, Singh G, Saini S. Fast dissolving films: a novel approach to oral drug delivery. Int Res J Pharm 2011;2:69-74
12. Kirsch K, Hanke U, Weitschies W. An overview of intestinal wafers for oral drug delivery. European Journal of Pharmaceutics and Biopharmaceutics. 2017 May 1;114:135-44.
13. Verena L, Garsuch K. Preparation and characterization of a fast dissolving oral films for paediatric use. Diisseldorf J HeinrichHeine University 2006;3;2-5.
14. Finch CA, editor. Chemistry and technology of water-soluble polymers. Springer Science & Business Media; 2013 Jun 29.
15. Costa JS, de Oliveira Cruvinel K, Oliveira-Nascimento L. A mini-review on drug delivery through wafer technology: Formulation and manufacturing of buccal and oral lyophilizates. Journal of Advanced Research. 2019 Nov 1;20:33-41.
16. Pathan IB, Setty CM. Chemical penetration enhancers for transdermal drug delivery systems. Tropical Journal of Pharmaceutical Research. 2009;8(2).
17. Lawrence MJ. Surfactant systems: their use in drug delivery. Chemical Society Reviews. 1994;23(6):417-24.
18. Bhattarai M, Gupta AK. Fast dissolving oral films: a novel trend to oral drug delivery system. Sunsari Technical College Journal. 2015;2(1):58-68.
19. Douroumis D. Practical approaches of taste masking technologies in oral solid forms. Expert opinion on drug delivery. 2007 Jul 1;4(4):417-26.
20. Tao D, Wang T, Wang T, Qu X. Influence of drug colour on perceived drug effects and efficacy. Ergonomics. 2018 Feb 1;61(2):284-94.
21. Emmelin N, Engström J. Effect of sympathetic denervation on the sensitivity of the submaxillary gland to stimulating agents. The Journal of Physiology. 1960 Aug;153(1):9.
22. Fox PC. Salivary enhancement therapies. Caries research. 2004;38(3):241-6.
23. Ali S, Quadir A, High molecular weight povidone polymer-based films for fast dissolving drug delivery applications. Drug Delivery Technology. 2007 (6): 36–43.
24. Frey HK. Film strips and pharmaceuticals. Pharm Manufacturing Packing Sourcer 2006;6:92-93.
25. Mandeep K, Rana AC, Nimrata S. Fast Dissolving Films: An Innovative Drug Delivery System. International Journal of Pharmaceutical Research & Allied Sciences. 2013 Jan 1;2(1).
26. Repka MA, Baltu JK, Upadahay SB, Tunma S. Pharmaceutical application of holt-melt extrusion part. Drug Dev Ind Pharm 2007;33:909-26.
27. Bhyan B, Jyangra S, Kaur M, Singh H. Orally fast dissolving films: innovations in formulation and technology. Int J Pharm Sci Rev Res 2011;9:50-7.

28. Kate VK, Payghan SA, Shinde AJ. Effect of ageing condition on the dissolution stability of piroxicam mucoadhesion fast disintegrating tablet. Inventi Rapid NDDS 2013;5:455-8.
29. Mooter GVD. The use of amorphous solid dispersions: A formulation strategy to overcome poor solubility and dissolution rate. Drug Discovery Today 2011;9:975-81.
30. Maniruzzamam M, Boateng J, Bennefille M. Taste masking of paracetamol by holt-melt extrusion: An imino&invitro evaluation. Eur J Pharm Biopharm 2012;80:433-42
31. Bhalla HL. Drug delivery research in India a challenge and opportunity. J Controlled Release 1999;62:65-8
32. Boateng JS, Matthews KH, Auffret AD, Humphrey MJ, Stevens HN, Eccleston GM. In vitro drug release studies of polymeric freeze-dried wafers and solvent-cast films using paracetamol as a model soluble drug. International Journal of Pharmaceutics. 2009 Aug 13;378(1-2):66-72.
33. Kolteo K, Maschke A. Melt extrusion for pharmaceuticals. Int J Execrative-Acta 2009;22:2-5.
34. Sushmitha S, Priyanka SR, Krishna LM, Murthy MS. Formulation and evaluation of mucoadhesive fast melt-away wafers using selected polymers. Research Journal of Pharmacy and Technology. 2014;7(2):176-80.
35. Lim SC, Paech MJ, Sunderland B, Liu Y. In vitro and in vivo evaluation of a sublingual fentanyl wafer formulation. Drug Design, Development and Therapy. 2013 Apr 12:317-24.
36. Reddy D, Choonara YE, Kumar P, Govender M, Indermun S, Du Toit LC, Meyer LC, Pillay V. In vivo evaluation of an Ultra-fast Disintegrating Wafer matrix: A molecular simulation approach to the ora-mucoadhesivity. Journal of Drug Delivery Science and Technology. 2017 Feb 1;37:123-33.
37. Thakur RR, Rathore DS, Narwal S. Orally disintegrating preparations: recent advancement in formulation and technology. Journal of Drug Delivery and Therapeutics. 2012 May 14;2(3).
38. Mehravaran M, Haeri A, Rabbani S, Mortazavi SA, Torshabi M. Preparation and characterization of benzydamine hydrochloride-loaded lyophilized mucoadhesive wafers for the treatment of oral mucositis. Journal of Drug Delivery Science and Technology. 2022 Dec 1;78:103944.
39. Troester MM, Hastriter EV, Ng YT. Dissolving oral clonazepam wafers in the acute treatment of prolonged seizures. Journal of child neurology. 2010 Dec;25(12):1468-72.
40. El-Mahrouk GM, El-Gazayerly ON, Aboelwafa AA, Taha MS. Chitosan lactate wafer as a platform for the buccal delivery of tizanidine HCl: in vitro and in vivo performance. International journal of pharmaceutics. 2014 Jun 5;467(1-2):100-12.
41. Adelman JU, Mannix LK, Von Seggern RL. Rizatriptan tablet versus wafer: patient preference. Headache: The Journal of Head and Face Pain. 2000 May;40(5):371-2.

42. Hajhashemi H, Taymouri S, Shafiee F. Development and evaluation of wafer loaded with sertaconazole solid dispersion for the treatment of oral candidiasis. Brazilian Journal of Pharmaceutical Sciences. 2023 May 15;59:e22452.
43. Chakraborty P, Dey S, Parcha V, Bhattacharya SS, Ghosh A. Design expert supported mathematical optimization and predictability study of buccoadhesive pharmaceutical wafers of loratadine. BioMed research international. 2013 Jan 1;2013.
44. Shapira-Furman T, Serra R, Gorelick N, Doglioli M, Tagliaferri V, Cecia A, Peters M, Kumar A, Rottenberg Y, Langer R, Brem H. Biodegradable wafers releasing Temozolomide and Carmustine for the treatment of brain cancer. Journal of controlled release. 2019 Feb 10;295:93-101.
45. Gururangan S, Cokgor I, Rich JN, Edwards S, Affronti ML, Quinn JA, Herndon JE, Provenzale JM, McLendon RE, Tourt-Uhlig S, Sampson JH. Phase I study of Gliadel™ wafers plus temozolomide in adults with recurrent supratentorial high-grade gliomas. Neuro-oncology. 2001 Oct 1;3(4):246-50.
46. Mehravaran M, Haeri A, Rabbani S, Mortazavi SA, Torshabi M. Preparation and characterization of benzydamine hydrochloride-loaded lyophilized mucoadhesive wafers for the treatment of oral mucositis. Journal of Drug Delivery Science and Technology. 2022 Dec 1;78:103944.
47. Vaezi H, Rabbani S, Mortazavi SA, Kamalinejad M, Haeri A. Fabrication, in Vitro, and in Vivo Characterization of Mucoadhesive Berberine-Loaded Blended Wafers for Treatment of Chemotherapy-Induced Oral Mucositis. AAPS PharmSciTech. 2022 Dec 16;24(1):19.
48. Mostafa DA, Hashad AM, Ragab MF, Wagdy HA. Comparison between the pharmacokinetics data of ketorolac Tromethamine wafer a novel drug delivery system and conventional ketorolac Tromethamine tablets to enhance patient compliance using a new LC-MS/MS method. BioNanoScience. 2020 Sep;10:745-57.
49. Márquez-Rivas J, Ramirez G, Ollero-Ortiz Á, Giménez-Pando J, Emmerich J, Quiroga-Cantero E, Rivas E, Gómez-González E. Initial experience involving treatment and retreatment with carmustine wafers in combination with oral temozolomide: long-term survival in a child with relapsed glioblastoma multiforme. Journal of Pediatric Hematology/Oncology. 2010 Jul 1;32(5):e202-6.