IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

A CURRENT DRUG DELIVERY SYSTEM: FORMULATION AND DEVELOPMENT IN ORALLY DISINTEGRATING FILM

Ankit Vijay[1*], Dr. Shiv Garg[2], Dr.Piush Sharma[2], Dr.Vishal Garg[3]

[1*] Research Scholar, Maharishi Arvind College of Pharmacy, Jaipur, Rajasthan

[2*] Professor, Maharishi Arvind College of Pharmacy, Jaipur, Rajasthan

[3*] Principal, Jaipur School of Pharmacy, MVGU, Jaipur, Rajasthan

ABSTRACT

Over years, inclination towards inventive medicine conveyance systems has interestingly extended attempts to guarantee efficacy, security and patient worthiness. With respect to course of medication organization many substitutes have reliably been presented by using ongoing novel advancements for pediatrics, geriatrics, sick and rebelliousness patients. Orally dissolving films (ODFs) give uick release of an active pharmaceutical ingredient (API) when put on the tongue. ODFs give an option to orally disintegrating tablets. These portion structures are placed on a patient's tongue or any oral mucosal tissue. Right when wet by salivation, the film rapidly hydrates and follows onto the site of use.It rapidly deteriorates and breaks up to convey the prescription for mucosal ingestion or with changes, considers oral gastrointestinal digestion with quick dissolving properties. Consequently, research in growing orally disintegrating systems has been planned at investigating different excipients as well as strategies to meet these faces. A combination of estimations structures like tablets, films, wafers, gnawing gums, microparticles, nanoparticles, etc have been made for further developing the show credits in the orally deteriorating media.

KEYWORDS

Orally dissolving films, Oral gastrointestinal assimilation, Oral mucosal tissue, Disintegration, Active Pharmaceutical Ingredients.

[A] Introduction

Orally disintegrating films (ODF) has one of the most popular forms of medication administration because of its amazing patient accommodation and consistence. The prime advantage of the estimation structure rises up out of fast disintegration: it will in general be placed on the tongue without the need of water.

Intraoral route is the most liked because of its comfort and rapid onset of activity. Intraoral portion structures have created as a choice rather than customary tablets, containers and liquid definition. Of the intraoral measurement's structures, fast dissolving dose structures have obtained a great deal of thought in view of worked with persistent consistence and effortlessness of association. Issues related with standard estimations structures like disintegration and bioavailability of medication particles can be overpowered with subtleties expected for progastrin conveyance. [1].

The potential gain of using ODF is the high adequacy of osmosis of specific blends by oral through without the need of water for swallow, being a choice as opposed to bioactive directed in tablets and pills [1,2], and what's more the ingestion through the buccal epithelium, without contact with gastrointestinal bundle which could ruin a few sensible compounds [3].

The administration of ODFs enjoys various benefits and some of them are as per the following:

i. Easy transportation.
ii. Ease of swallowing for geriatrics and paediatrics
iii. Convenient and accurate dosing
iv. No need of water for administration.
v. Convenient for dysphasic patients having difficulty in swallowing tablets and capsules.
vi. Rapid onset of action with increased bioavailability due to bypassing hepatic first pass effect and stability

No costly lyophilization, high mechanical strength, rapid disintegration are the quality credits of ODF have accomplished momentous importance in drug industry for the explanation of having special properties and quick disintegration, time going from seconds to one moment ODFs configuration grants to fuse an assortment of medications for their pharmacological effects e.g., anti-tussive, anti-epileptic, anti-asthmatic, expectorant, etc. High temperature and moisture [4].

Disadvantages:

1. Dose uniformity is a technical challenge.
2. Require special packaging for products stability and safety.
3. High doses cannot be incorporated (<40 mg/4cm^2 piece)
4. Hygroscopic in nature.

[B] Formulation:

ODFs are fast disintegrating thin films having an area vacillating from 5 to 20 cm^2 in which drug is integrated in the form of matrix using hydrophilic polymer. Active pharmaceutical ingredient can be included up to 15 mg with other excipients i.e., plasticizers, colorants, sweeteners, taste masking agents, etc. Plasticizer increases workability, Spreadability and flexibility of films. [5]

Components	Conc. (%)
Active pharmaceutical ingredient	1–25
Hydrophilic polymer	40–50
Plasticizer	0–20
Colour, filler, flavour	0–40

[B.1.] Active pharmaceutical ingredient:

Various classes of drugs can be incorporated into ODFs e.g., anti-histamine, anti-diarrheal, anti-depressants, vasodilators, anti-asthmatic, anti-emetic, etc [6]. Dimenhydrinate can also be incorporated into ODFs for taste masking. drugs incorporated into ODFs are salbutamol sulphate, rizatriptan benzoate, verapamil, ondansetron, dexamethasone, cetirizine, pilocarpine, tianeptine sodium, indomethacin, etc.

[B.2.] Hydrophilic polymers:

The improvement of an ODF is an element of advocated choice and convergence of polymers as the mechanical strength of films is emphatically connected with these elements. The veracity of fast dissolving oral films is dependent upon careful selection of polymer nature and concentration. Generally, polymer concentration used in preparing ODFs is around 45% w/w of total weight of dry thin strip, though, it can be increased up to 60–65% w/w in order to accomplish the film of characteristics and attributes. [7]

Properties

- Non-irritant
- Should not hinder with the disintegration time of ODF
- Non-toxic
- Non-irritant
- Affordable
- Should possess adequate shelf-life
- Should possess good spread ability
- Should exhibit sufficient tensile strength
- Should have good mechanical properties

[B.3.] Plasticizers

In general, mechanical properties, for example, rigidity and percent extension are improved by adding plasticizer to the definitions. The convergence of plasticizer ordinarily goes from 0% to 20% w/w. Normal instances of plasticizers are PEG, glycerol, diethyl phthalate, triethyl citrate, tributyl citrate, and so forth.

[B.4.] Sweetening Agent

Sweeteners have developed an imperative part of the food products as well as pharmaceutical products projected to be disintegrated or dissolved in the oral cavity. Natural sweeteners as well as artificial sweeteners are used to increase the palatability of the mouth dissolving formulations.

Sweetening agent	Example
Natural	Glucose, fructose, dextrose, sucrose, and isomaltose
Artificial	Acesulfame-K, sucralose, and neotame

[C] Conventional approaches for manufacturing of ODFs :

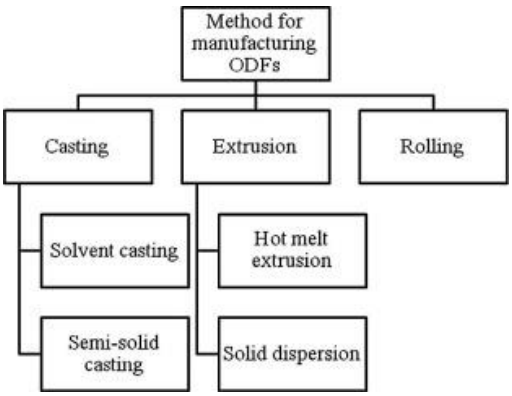

Figure 1. Conventional approaches for manufacturing ODFs.

[C.1] Solvent casting method

Solvent casting is the most by and large used procedure for the preparation of ODFs using water dissolvable excipients, polymers and prescription which are separated in de-ionized water; in this way, a homogenous blend is gotten by applying high shear powers created by a shear processor. Then, the arrangement is poured onto petri plate and the dissolvable is allowed to dry by introducing it to high temperature to accomplish incredible quality film. [8]

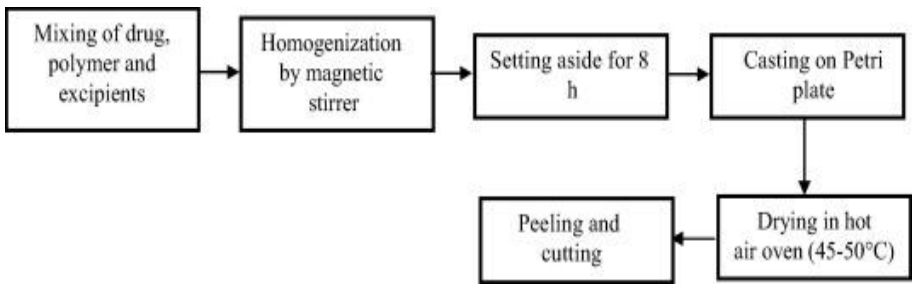

Figure 2. Flow chart of solvent casting method

[C.2] Semi-solid casting method

In this method, solution of water-soluble film forming polymer is assorted to solution of acid insoluble polymer to form homogenous viscous solution (e.g. cellulose acetate phthalate and cellulose acetate butyrate).

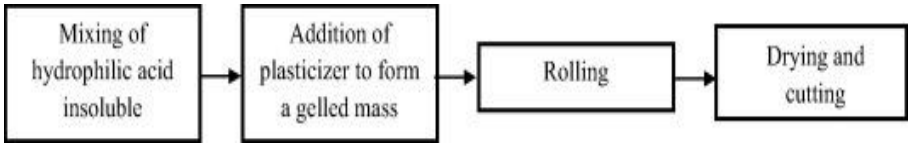

Figure 3. Flow map of semi-solid casting method

[C.3] Hot melt extrusion

Processing films by this technique, involves shaping a polymer into a film via the heating process rather than through the traditional solvent casting technique.

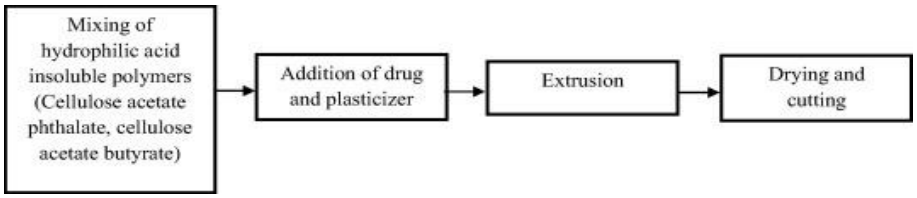

Figure 4. Flow chart of hot melt extrusion method.

This is a solvent free process, notwithstanding, the handling of thermolabile substances is a significant disadvantage of this cycle because of the utilization of high temperature during extrusion. [9]

[D] Characterization and Evaluation

1. Organoleptic evaluation

Remarkable controlled human taste bud is used for such explanation. This in vivo taste appraisal is finished on human workers. In-vitro taste evaluation of ODFs is performed by using taste sensors for screening. In vitro taste assessing methods and progressions are legitimate and satisfactory for high-throughput taste distinguishing of such portion structures. Both in vivo and in vitro methodologies take apart the taste hiding limit and loveliness level of taste covering trained professionals.

2. Thickness test

Thickness of a film is constrained by using changed progressed micrometer and thereafter consequently mean not entirely settled. Three readings from all of the still up in the air. Weight variety of a not entirely settled in that frame of mind by cutting the film and film and deciding load of each film. Consistency in thickness is basic to anyway certain as it is by all accounts straight forwardly comparative with segment precision of the film.

3. Tensile strength

Tensile strength is characterized as greatest pressure applied at which the film breaks. Essentially, this test is performed to gauge the mechanical strength of films. It tends to be determined from applied burden at break partitioned by the strip cross-sectional region given in the equation below:

Tensile strength = (load at failure / strip thickness * strip width) * 100

4. Percentage elongation:

When the sample films are subjected to tensile stress, deformation of the films occurs resulting in stretching or elongation of sample. It is performed to predict the ductility of polymers using a texture analyser. It is calculated by formula:

% Elongation = Increase in length ×100 / Original length

5. Swelling property:

Simulated saliva solution is used to check the swelling studies of films. Initial weight of film is governed and is located in pre-weighed stainless steel wire mesh. This mesh containing film is then dipped into simulated saliva solution. Increase in the weight of film is observed at constant pre-determined time intervals until no more increase in weight. Degree of swelling is defined by these parameters:

Degree of swelling = final weight (wt) –Initial weight (w0)/ Initial weight (w0)

Wt = weight of film at time interval t, w0 = weight of film at time 0.

6. Transparency

Transparency of a strip is decided by using a UV-spectrophotometer. This test is accomplished for visual appearance of the formulation. Film specimen are cut into rectangular shapes and positioned on the internal side of the photometer cell. Transmittance of the film is functioned out at 600 nm wavelength.
Transparency=(logT600)/b=-€c
T600 = transmittance at 600 nm, *b* = film thickness (mm), and *c* = concentration.

7. Content uniformity

Contents of a film are settled by standard measure strategy determined for explicit medication in various pharmacopeia. This test is performed on 20 examples utilizing scientific strategies. The acknowledgment worth of the test is under 15% as per Japanese pharmacopeia. As per USP27, the items ought to reach from 85% to 115% with the standard deviation of not exactly or equivalent to 6%.

8. Disintegration time

Disintegration apparatus quoted in official pharmacopoeias is used for governing the disintegration time of a film. Normally, the disintegration time is the function of composition of film as it varies with the formulation and generally reaches from 5 to 30 s. Mostly, the USP disintegration apparatus is used for this test. There are two methods for determining disintegration time of film:

Slide frame method

A drop of distilled water is poured onto the film clamped into slide frames placed on petri dish. Time taken by the film to dissolve is noted. [12]

Petri dish method

A film is placed onto 2 ml distilled water taken in petri dish. Time taken by the film to dissolve completely is considered as the disintegrating time.[13]

9. In-vitro dissolution test:

Standard official basket or paddle apparatus is used for directing dissolution studies on films. Sink conditions should be retained during dissolution. Sometimes while performing this process, film floats over the medium making it difficult to perform the test properly. This problem is more likely to occur in case of paddle method thus the basket apparatus is mostly preferred. Media used are 6.8 pH phosphate buffer (300 ml) and 0.1 N HCl (900 ml). Temperature is maintained at 37 ± 0.5 C and rotation speed of 50 rpm is usually adjusted. Samples of drug dissolved are collected at pre-determined intervals and are analyzed by using UV-spectrophotometer. [10, 11]

[E] Conclusion

The ongoing study shows that ODFs are one of the novel approaches in the field of drug sciences. They have additionally evolved affirmation and patient consistence with no risk of choking related with better prosperity and reasonability correlation with standard portion structures. The essential idea behind plan of ODFs was to adjust to the difficulty in swallowing common oral measurements structures among paediatric, geriatric and mental patients with dysphagia. By and by, ODFs are by and large available for hypertension, acridity, awareness, torture, etc reflecting their importance. Critical advantages of such portion structure are their association without the use of water fulfilling the need of target people searching for convenience in drug organization close by bypassing the hepatic assimilation, consequently, prompting worked on restorative reaction.

[F] References

1. Pfister W, Ghosh T, Intraoral delivery systems: An overview, current status and future trends. In Tapash Ghosh, William Pfister (Ed.), Drug Delivery to the Oral Cavity: Molecules to Market (pp.1-34). Florida: CRC Press, Taylor & Francis gp, 2005.
2. Liang AC, Chen LH, "Fast Dissolving Intraoral Drug Delivery Systems",Exp. Opin. Ther. Patents, 11(6), 981–986, 2001.
3. Mishra R, Amin A, "Formulation development of taste masked rapidly dissolving films of cetirizine hydrochloride", Pharm Tech (USA), 33(2), 48-56, 2009.Bai, G., Armenante, P.M., Plank, R.V., Gentzler, M., Ford, K., Harmon, P., 2007. Hydrodynamic investigation of USP dissolution test apparatus II. J. Pharm. Sci. 96, 2327–2349.

4. Arya et al., 2010 A. Arya, A. Chandra, V. Sharma, K. Pathak Fast dissolving oral films: an innovative drug delivery system and dosage form Int. J. Chem. Tech. Res., 2 (2010), pp. 576-583.

5. M. Preis, M. Pein, J. Breitkreutz Development of a taste-masked orodispersible film containing dimenhydrinate Pharmaceutics, 4 (2012), pp. 551-562

6. Chauhan, M. Yasir, P. Nagar Insights into polymers: film formers in mouth dissolving films Drug Invent. Today, 3 (2012), pp. 56-73

7. D.R. Choudhary, V.A. Patel, U.K. Chhalotiya, H.V. Patel, A.J. Kundawala Development and characterization of pharmacokinetic parameters of fast-dissolving films containing levocetirizine Sci. Pharm., 80 (2012), pp. 779-787

8. R.R. Thakur, D.S. Rathore, S. Narwal Orally disintegrating preparations: recent advancement in formulation and technology J. Drug Deliv. Therap., 2 (3) (2012), pp. 87-96

9. Kunte S, Tandale P. Fast dissolving strips: A novel approach for the delivery of verapamil. J Pharm Bio Sci. 2010;2(4):325-328.

10. Ramani C.C., Puranik P.K., Dorl A.K. Study of diabetic acid as matrix forming material. Int J Pharm. 1996; 137:11-19.

11. Wu Y, Weller C, Hamouz F, Cuppett S, Schnepf M. Moisture Loss and Lipid Oxidation for Precooked Ground-Beef Patties Packaged in Edible Starch-Alginate-Based Composite Films. Journal of Food Science. 2001;66(3):486-493.

12. El-SetouhyDEl-Malak N. Formulation of a Novel Tianeptine Sodium Orodispersible Film. AAPS PharmSciTech. 2010; 11(3):1018-1025.