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ORODISPERSIBLE FILMS – THE ADVANCEMENT IN DRUG DELIVERY SYSTEM

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ABSTRACT

Oral drug delivery using orodispersible films is becoming more prevalent. While breath fresheners and over-the-counter treatments have long been popular in the United States, the first prescription medication films were only recently released to the European and American markets. The FDA has already designated oral soluble film as a distinct Rx (prescription medication) dosage for, and such products are not interchangeable with traditional oral dosage forms. Orodispersible film is the official name used by the European Medicines Agency (ODF). The breadth of ODF technology and its benefits over traditional dosage forms suggest that ODFs will be used in more applications and commercialized goods in the near future. As a result, authorities must issue an ODF monograph as soon as feasible in order to harmonize characterization methodologies and quality requirements.[7] This articles aims to compile some of the exclusive approaches of formulation and evaluation of ODF to in an article.

INTRODUCTION

ODF have the ability to offer customize treatments to a variety of patient groups. Due to their greater flexibility and comfort, fast dissolving oral films (FDOFs) are the most sophisticated kind of oral solid dose form. Because mouth dissolving films offer more convenience and simplicity of use than other dosage forms such as orally disintegrating tablets, buccal tablets, and sublingual tablets, mouth dissolving films are attracting the attention of a growing number of pharmaceutical companies. An excellent film should have qualities such as a pleasing taste, high stability, simplicity of handling and administration, and the capacity to be applied without the need of water. Because the medication disintegrates quickly and dissolves in the saliva without the use of water, the fast dissolving drug delivery system has a significant advantage over Traditional dose forms. Despite the disadvantage of delayed start of action, these oral dosage forms have a number of advantages, including self-medication, greater compliance, convenience of manufacture, and the absence of discomfort. As a result, fast disintegrating tablet (FDT) technology is gaining traction these days, with a large range of medicines fulfilling a variety of objectives. [1, 2]

Review of Literature:

Orodispersible films (ODFs) are a potential medication delivery method for small-scale pharmaceutical preparations on a small scale. The goal of the research was to provide a flexible casting solution that could be used to make ODFs quickly and with active pharmaceutical ingredients (APIs). The appropriateness of various combinations of film forming agents and other excipients, as

well as various casting heights, for the manufacture of ODFs was investigated. Hypromellose, carbomer, glycerol, disodium EDTA, and trometamol were shown to be the best casting solution.This casting solution was used to make ODFs with water-soluble APIs (enalapril maleate and prednisolone disodium phosphate) and a weakly water-soluble API (diazepam) that was co-solvented with ethanol 96 percent. The viscosity of the casting solution, mechanical characteristics, and disintegration time of the ODFs were all affected by water-soluble APIs and ethanol. The European Pharmacopoeia (2014) (Ph. Eur.) 8th edition specified standards for uniformity of mass and homogeneity of composition for all ODFs incorporating API. In conclusion, pharmaceutical-grade ODFs may be made on a modest scale. As a result, the possibility of employing ODFs for personalised medication has emerged.[3]

Orodispersible films (ODFs) are a useful dosage form for improving patient comfort and concordance with oral medication administration. They have a variety of unique application characteristics, such as the capacity to be administered without the need of water and appropriateness for individuals with swallowing difficulties. However, until now, this potential dosage form has only been available in immediate release formulations. A thin film made by solvent casting that dissolves quickly in the mouth but offers sustained drug release by containing drug-loaded matrix particles (MPs). MPs were made utilising theophylline anhydrous as a model drug and Eudragit® RS as a matrix-forming agent to allow for extended drug release. The film former used in the production of ODFs was hypromellose. The kinetics and duration of drug release were investigated using dissolution experiments. The disintegration time was also measured using a PharmaTest® disintegration analyzer with an ODF-specific sample container.[4]

Natural (xanthan gum), semisynthetic (hydroxypropyl methylcellulose and hydroxyethyl cellulose), and synthetic (polyvinyl alcohol) polymers were used to make a fast dissolving orodispersible film (ODF) for simultaneous administration of biopharmaceutical classification system (BCS) class II drugs, meloxicam (MX) and tizanidine (TZ). The components of ODFs were tested for compatibility using Fourier transform infrared spectroscopy and differential scanning calorimetry.Disintegration time, pH of the film surface, tensile strength, folding endurance, percent elongation, and content uniformity (MX and TZ) were measured and found to be in the range of 171.3–563.1 s, 5.110.07–6.280.05, 14.7211.2–33.0843.1 N/m2, > 100, 3.330.53–10.040.77 percent and 98.01–99.34 percent (MX) and 97.48–99. All formulations had moisture absorption, moisture loss, and loss on drying values ranging from 1.060.09–7.510.93%, 0.060.01–2.30.08%, and 0.0080.002–0.030.03%, respectively.In an in vitro drug release assay in simulated saliva fluid at pH 7.4, > 90% of MX and TZ were released in 5 minutes. The flat surfaces of all ODFs were revealed by visual inspection, scanning electron microscopy, and X-ray diffraction analysis. In comparison to other formulations, ODF made from xanthan gum (F5) showed improved physicochemical and mechanical characteristics.[5]

Orodispersible films (ODF) offer therapeutic promise as personalised pharmacological extemporaneous pharmacy formulations. However, due to content consistency problems originating from viscosity variations in the casting solution and variable operator manipulation, the traditional technique of ODF production employing a film applicator may limit its use. The unit-dose (UD) plate is proposed as an alternative to the film applicator for compounding individual ODFs in this study. A n extemporaneous ODF formulation for the antiemetic medication ondansetron hydrochloride dihydrate (OND) at a therapeutically appropriate dosage using a design-of-experiments method was prepared.The content homogeneity of ODFs cast with the UD plate was good, regardless of the viscosity of the casting fluid or drug concentration. The performance of the formulations was assessed in terms of patient acceptance and product quality. The impact of important process factors on ODF quality characteristics was investigated. The primary variables impacting disintegration time and

mechanical characteristics of the film were HPMC concentration and volume of casting solution, whereas drug concentration had no influence. [6]

A research was conducted with the goal of developing orodispersible film(s) of the antidepressant medication tianeptine sodium for geriatric and paediatric patients to improve convenience and compliance. The novel film former, lycoat NG73 (granular hydroxypropyl starch), was tested alongside other film-forming agents (hydroxypropyl methyl cellulose, hydroxyethyl cellulose, and polyvinyl alcohol), as well as three film modifiers (maltodextrin, polyvinyl pyrrolidone K90, and lycoat RS780 (pregelatinized hydroxypropyl starch).The in vitro dissolving parameters, in vitro disintegration time, and physico-mechanical properties of eight formulas were examined using the solvent-casting method. In rabbits, the bioavailability of a promising orodispersible film based on lycoat NG73 (F1), which showed the greatest drug dissolution, satisfactory in vitro disintegration time, and physico-mechanical properties suitable for orodispersible films, was compared to a reference marketed product (Stablon® tablets). There was no significant difference in the bioavailability parameters of the test film (F1) and the reference product (C max (ng/ml), t max (h), AUC0–t (ng h ml1), and AUC0– (ng h ml1)] according to statistical analysis.C max (89.74%), AUC0–t (110.9%), and AUC0– (109.21%) mean ratio results (test/reference) revealed that the two formulas had similar plasma level-time profiles. These findings imply that tianeptine-containing rapid orodispersible films will likely become a popular therapeutic option for acute depression.[8]

A research was undertaken to develop and assess microparticles that were to be used in the manufacture of two orodispersible dosage forms to conceal the bitter taste of prednisolone. Spray-drying was used to make microparticles based on Eudragit E PO or E 100 as a taste-masking agent. A single-punch tablet press was used to compress tablets containing microparticles, co-processed ODT excipient Pharmaburst, and lubricant. Casting polymeric solutions of hydroxypropyl methylcellulose containing evenly distributed microparticles resulted in orodispersible films. For formulated dosage forms, physicochemical characteristics of micro particles as well as mechanical properties analysis, disintegration time measurements, and dissolving tests were assessed. Microparticles containing Eudragit E 100 had good masking capabilities in dissolving experiments. In phosphate buffer 6.8, the quantity of prednisolone released within the first minute was about 0.1 percent. The quantity of released prednisolone increased significantly after integration into orodispersible forms. It was most likely the result of quicker microparticles soaking in orodispersible forms and being partially destroyed during the tableting process by compression force.[9]

Oral solid dose forms such as orodispersible film (ODF) are frequently utilised. It is not however, appropriate for medicines having a short half-life, bitterness, or high hygroscopicity. The aim of research was to create a betahistine hydrochloride ODF with long-term stability and no bitterness. Batch technique was used to make the drug–resin complex (IRDC). To evaluate the differences between ODF containing IRDC and ODF containing betahistine hydrochloride, an in vitro dissolving experiment, an e-Tongue test, and a hygroscopicity test were performed. The rate-limiting phase of drug release was found to be drug diffusion in the IRDC, according to drug release kinetics. The molecular mechanism of taste masking and hygroscopicity decrease was investigated using DSC and FT-IR. Taste masking was discovered to be caused by an ionic interaction between the drug and the resin, as well as the drug's delayed dissolution from the IRDC. Drug–resin interaction occupies the location where the drug forms hydrogen bonds with water molecules, resulting in hygroscopicity decrease. In conclusion, not only a betahistine hydrochloride ODF with good characteristics was created, but also investigated the impact of drug–resin interaction on sustained release, taste masking, and hygroscopicity reduction in this work.[10]

It is necessary to have biorelevant methodologies for studying the breakdown of pharmacological orodispersible dose forms. In vitro techniques that combine biorelevant quantities of disintegration medium and mechanical stressors that replicate in vivo circumstances should be used to assess orodispersible disintegration. A research suggests the use of a mechanical oral cavity model to investigate the breakdown of orodispersible films. In the presence of a biorelevant volume of artificial salivary fluid, the sample is compressed on a regular basis.During disintegration, four orodispersible film samples (P1, C1, P2, and C2) with different polymer types and molecular weights, as well as Listerine®, were tested and filmed. The volume reduction of the film matrix over time was determined using an image analysis tool as a descriptor of film disintegration behaviour. P1 and Listerine® had a volume decrease of >90% at 180 s, while C1, P2, and C2 had volume reductions of 85 percent, 48 percent, and 37 percent, respectively. The model was able to distinguish between the four samples' disintegration behaviour, and the results were equivalent to the benchmark product.For the first time, the notion of orodispersible film disintegration behaviour was proposed as an instructive technique for the research of orodispersible dosage forms.[11]

The goals of a study were to design a dissolving test technique that could be used to evaluate the drug release of film preparations with immediate and modulated release profiles, as well as to investigate the test setup's potential by taking into account various physiological factors. As a result, a standard flow-through cell was outfitted with custom-made sample containers. One of the sample holders was prototyped using three-dimensional printing technology. ODFs with immediate (ODFIR) and extended release (ODFPR) properties, as well as a double-layer film (ODFDL) with a water-insoluble shielding layer, were studied. For all film types, anhydrous theophylline was utilised as a model medication. The drug release behaviour of oral film preparations with immediate and modulated release characteristics can be successfully determined by adding specific fittings for oral films to a standard flow-through cell. In the case of ODFDL, the use of film sample holders with backing plates, such as the film sample holder with backing plate (FHB) and the 3D printed film sample holder (FH3D), resulted in longer release profiles, with 14.6 1.30 percent theophylline dissolved within 2 hours for FHB versus 92.9 3.33 percent for the film sample holder without backing plate (FH). This demonstrates their appropriateness for examining the shielding layer's integrity. Due to a lower ODF surface exposed to the dissolving medium, the application of the backing plate further reduced drug release of ODFPR 315 to 61.0 1.69 percent dissolved theophylline within 2 h using FHB compared to 82.3 0.74 percent using FH. Using varied flow rates and medium compositions to replicate circumstances within the oral cavity, stomach, and intestine, the potential of the dissolution test setup to consider physiological parameters of the human gastrointestinal transit was examined. Reduced theophylline release was detected at a low flow rate of 1 ml/min, which is comparable to salivary flow within the oral cavity, whereas similar release patterns were found at flow rates of 2 and 8 ml/min. Changing the composition of the dissolving media has a significant influence on theophylline release. Because ODFPR drug release is governed by diffusion across a water-insoluble matrix, ion species and concentration have a significant impact on release behaviour. IVIVC experiments will be conducted in the future to see if the data gained can be utilised to predict drug release behaviour of ODFs during human gastrointestinal transit.[12]

Due to the flexible and precise character of the methods, several printing technologies have lately been investigated in the pharmaceutical area. The goal of this study was to compare two new printing processes with the present approach for producing patient-tailored warfarin dosages at HUS Pharmacy in Finland. Semisolid extrusion 3D printing, inkjet printing, and the known compounding method for oral powders in unit dose sachets were used to create dosage forms of various strengths (0.1, 0.5, 1, and 2 mg)

(OPSs). Using hydroxypropylcellulose as a film-forming agent, orodispersible films (ODFs) drug-loaded with warfarin were printed. The OPSs were made up of commercially available warfarin tablets and a filler called lactose monohydrate. The ODFs produced thin, flexible films with satisfactory ODF characteristics. Furthermore, as compared to the established OPSs, the printed ODFs had higher drug content. During the one-month stability testing, all dose forms were shown to be stable and appropriate for administration through a naso-gastric tube, allowing administration to all potential patient groups in a hospital ward.[13]

To increase oral bioavailability in multiple sclerosis therapy, researchers developed an oral film comprising biocompatible and biodegradable chitosan-alginate nanoparticles of DMF. The influence of different amounts of independent variables on important quality characteristics of films was examined, and film formulations including DMF were improved by design of experiments utilising complete factorial design. The orodispersible film of chitosan-alginate core-shell-corona shaped nanoparticles of DMF was made by ionotropic pre-gelation of the alginate core followed by chitosan polyelectrolyte complexation, and the resulting colloidal nanosuspension was added to the optimised polymer matrix composition by simple process integration and then cast to films by solvent casting process. pH, tensile strength, disintegration time, in-vitro drug release, ex-vivo permeation research via pig buccal mucosa, and in-vivo pharmacokinetic study in wistar rats were all used to evaluate the films. In comparison to DMF oral film formulations, which released more than 80 percent drug within 15 minutes, the in-vitro drug release profile from chitosan-alginate core-shell-corona shaped nanoparticles in film demonstrated a sustained release with an initial 18.39 percent release in 30 minutes followed by sustained release up to 6 hours. The in-vivo pharmacokinetic research revealed that nanoparticles of DMF in orodispersible films (DMF051) were 0.6-fold more bioavailable than traditional oral film formulation (DMF023) (30 mg of drug/film) even at extremely low drug concentration (2 mg/film). The Cmax values for DMF023 were 19.21 0.46 g/ml in comparison to 21.90 0.38 g/ml for DMF051 and 1.02 g/ml for drug suspension, Tmax values for DMF023 were 4.00 h in comparison to 2.00 h for DMF051, t1/2 values for DMF023 were 3.81 0.03 in comparison to 6.59 0.36 for DMF051, and AUC 0-t values for DMF023 were The study found that this potential dosage form had improved bioavailability, resulting in dose reduction and fewer adverse effects.[14]

The purpose of a study is to see if there is a link between the concentration of pullulan and the solubilizing agent and the disintegration time and drug release profile. As a film forming polymer and a solubilizing agent, pullulan and tween 80 were employed. The films were made and described using the solvent casting process. The optimal plasticizer and solubilizing chemical concentration was determined by the film's flexibility, tensile strength, and stickiness. Drug content and folding durability were best in fast dissolving films. The disintegration time of formulation PUT7 film was discovered to be 10 seconds, with in vitro release of 100% in around 90 seconds, which was faster than previous produced formulations. FTIR investigations of drug-excipient interactions revealed no interaction. The pH of the surface was determined to be neutral, indicating that administration was safe. All of the prepared films' physicochemical characteristics were unchanged after accelerated stability tests. As a result, the goal of developing atenolol rapid dissolving orodispersible films was accomplished.[15]

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