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A Review on Fast Dissolving Oral Films for Systemic Drug Delivery

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ABSTRACT -Oral fast disintegrating films is an emerging technology with rapid onset of action and improved patient compliance. It improvesthe efficacy of API's and provides better drug utilisation. These formulations are suitable for cold, allergic rhinitis, asthma attacks, CNS disorders where rapid onset of action is required for faster relief. The sublingual route of drug administration is very effective since the drug absorbed through the sublingual blood vessels by passes hepatic first pass metabolic process and gives a better bioavailability. The present article overviews the formulation aspects, manufacturing methodslike solvent casting,evaluation parameters and applications of fast dissolving films by sublingualroute.

Keywords: sublingual blood vessels, solvent casting

I. INTRODUCTION –

The most popular oral solid dosage forms are tablets and capsules. Many patients find it difficult to swallow tablets and hard gelatin capsules particularly pediatric and geriatric patients and do not take their medicines as prescribed. Difficulty in swallowing or dysphagia is seen to afflict nearly 35% of the general population. In some cases such as motion sickness, sudden episode of allergic attack or coughing, fear of choking and an unavailability of water, the swallowing of tablet or capsules may become difficult. To overcome these difficulties, several fast dissolving drug delivery systems have been developed(1)

Fast dissolving oral film is a novel advanced formulation for the large spectrum of drug and their delivery through oral route. These are very thin oral film which has a property to dissolve in the saliva within a minute. It is consider that dispersible formulation which taken into the mouth, get easily dispersed within 3 min. It is placed on the tongue and it releases the medication.(2,3,4)

OVERVIEW OF THE ORAL CAVITY -

The oral mucosa is composed of an outermost layer of stratified squamous epithelium. Below this lies a basement membrane, a lamina propria followed by the submucosa as the innermost layer. The oral mucosa in general is intermediate between that of the epidermis and intestinal mucosa in terms of permeability. It is estimated that the permeability of the buccal mucosais 4-4000 times greater than that of the skin. There are considerable differences in permeability between different regions of the oral cavity because of thediverse structures and functions of the different oral mucosa(5).

Technologies for manufacturing thinfilms (242243)-

The most commonly used techniquesfor the preparation ofthinfilms aresolvent casting (6,7)and hot melt extrusion (8,9). However, an innovative technique like inkjet printing (10)has evolved in thepastfew years. Various methods that have been employed for polymeric thin film manufacturing are described below in detail:

1. Solvent casting-

Among several techniques of film manufacturing, solvent casting is feasible, preferable and undoubtedly widely used method mainly due to the straightforward manufacturing process and low cost of processing. The manufacturingprocedure of thin films with the solvent castingmethod along with the quality control parameters in each step is illustrated in The rheological propertiesof the polymeric mixtureshould be taken into account since they affect the drying rate, the film thickness, the morphology as well the content uniformity of the films (11). The mixing process could introduce the air bubbles into the liquid inadvertently; therefore, de-aeration is a pre-requisite to obtain a homogeneous product (12). After casting the solution into a suitable substrate,

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they are left for drying to allowthe solvent to evaporatethat just leavesa polymeric film with a drug on it (13). After the complete drying of the film, it is cut into suitable shape and size depending upon the required dosage of the formed strip. Several advantages such as better physical properties, easy and lowcost processing, and excellent uniformity of thickness are observed with the film obtained by solvent-casting(14). However, this process suffers from some limitation. For instance, a polymeric thin film prepared by solvent casting method was brittle uponstorage, as marked by decrease in the percent elongation due to evaporation or loss of the residual solvent in the film over time

2. Hot-melt extrusion

HME is a versatile method adopted for the manufacture of granules, tablets, pellets (15), and alsothin films (8). It is a substitute method to solvent casting for the preparation of the film, especially useful when no organic solvent system is required (16). However, only fewliterature has reportedthe use of holt-melt extrusion for the preparation of polymeric thin films (17). HME is a process of shaping a mixture of polymers, drug substance, and other excipients into a film by melting all the components (18). Eventually,the films are cut into a particular shapeand dimensions (19). In this method, a mixture of pharmaceutical ingredients is molten and then charged through an orifice (the die) to obtainhomogeneous matrices. Since APIsare subjected to operation at high-temperature with complete absence of solvents, this method is not suitable for thermolabile APIs. The practical steps of HME areoutlined as follows(20) :(i) Feeding of the components to the extruder through a hopper,(ii) Mixing, grinding, and kneading,(iii) Flowing the molten and blended massto thedie,and(iv) Extruding the mass throughthe die and further downstream processing .With regards to the advantages of HME, it produces a drug in the form of solid dispersion or solution, which could improve solubility of poorly soluble drugs . However, atelevated temperature, there is a high chance of recrystallization of API in the polymer blend as the temperature drop. Using highly viscous molten polymer plasticizer can prevent this problem. Another issue of HME is “Die swell phenomenon” i.e. an increase in the cross-section of the film after ejection from the die depending on the viscoelasticcharacteristics of polymers. This is due to polymer withstanding high energy kneading and high shear force during extrusion. This problem can be prevented by slowing the speed of screw operation or by gently mixing molten mass for a long time instead of high shear kneading for a short duration . Unlike solvent casting, this method avoids the need of organic solvent; hence, they are proven to be environment friendly .

Printing technologies

Novel methods such as 3D printing could be used for manufacturingpolymeric thin films. It could potentially be a platform for producingthedosage form beneficial to the individual patient. This possibly will resolve the issue of the pharmaceutical industry and pharmacies to meet the future demand ofcustomized medicine(21). The printing technologies are increasinglygaining popularity because of its flexibility and cost-effectiveness.From the viewpoint of pharmaceutical industry, printing technologies are commonly in practice for identifying or labelling of the pharmaceutical dosage forms, particularly to optimize the product to be readily identified and to prevent counterfeit production. However, this approach has recently been adopted for the drug loading of pharmaceutical dosage forms . Theexamples include the use of off-the-shelf consumer inkjet printers in which drug-loaded inks are deposited to yield accurately dosed units of pharmaceutical ingredients. In addition, acombination of inkjet and flexographic technologies hasbeen practiced as well . The inkjet printing was used for printing of API on different substrate, whereas the flexographicprinting was employed to coat the drug loaded-substrate with a polymeric thinfilm (22).
To summarize, printing a drug on dosage form isthe latest interventionfor film preparationand it has become a powerful tool to manufacture dosage form with excellent uniformity, speed-ability, and stability. Representingprinting technologies that have been usedfor preparation of polymeric thin films are discussed below.

SEMISOLID CASTING

Insoluble polymer will be used in semisolid casting then in insoluble polymer add hydroxide (ammonium or sodium hydroxide). In this solution then add cellulose acetate butyrate and cellulose acetate phthalate. The acid insoluble polymer and film forming polymer used in the ratioof 1:4(23)

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SOLID DISPERSION EXTRUSION

In this method a drug dissolved in a liquid solventand then solution is incorporated into the polymer without removing the liquid solvent(23)

ROLLING METHOD

The drug which is containing the solution or suspension is rolled on the carrier. The solvent which is used in this process is mainly water and mixture of water and alcohol and then film is dried on the roller and then cut into a desired size and shape.(23)

EVALUATION PARAMETERS (24,25,26,27)

Thickness

The thickness of the patch was measured using digital Vernier Calliper with a least count of 0.01 mm at different spots ofthe film. The thickness was measured at three different spots of the patch and average was taken and SD was calculated.

2.Weight variation

Four centimeter square of the film was cut at three different places from the casted film. The weight of each film was taken and weight variation was calculated.

TENSILE STRENGTH

Tensile strength is the stress which is applied on the film and it continuous until it breaks the film. It is calculated by the given equation

Tensile strength = load at breakage/strip thickness ×strip width1

PERCENT ELONGATION

Strain is the force which is applied on the film and by this force the film will be stretched it also exhibits the strength of the film which it can bearafter applying force through jaws of the machine. Deformation of the film divided by original dimension of the sample that is strain. Elongation and plasticizer are depend on each other.

Percent elongation = L×100/Lo

Where, L= increase in length of film

Lo= initial length of film1

FOLDING ENDURANCE

The film is taken and then it is folded repeatedly in one direction and in opposite direction, this process is performed with the formulation until it breaks and then folding endurance is recorded by counting no of folds.

SURFACE PH -

It was determined by placing the film on the agar gel (1.5% w/v), then the pH probe is used to determine the pH of the prepared oral film formulations.

In vitro dissolution studies

Dissolution profile of fast dissolving films was carried out using USP type II (paddle apparatus) with 300 mL of simulated salivary fluid (pH 6.8) as dissolution medium maintained at 37 ± 1˚C. Medium was stirred at 100 rpm. Samples were withdrawn at every 30 sec interval, replacing the same amount with the fresh medium. Amount of drug in the withdrawn samples was determined by UV spectrophotometer. The percent drug released was plotted against time.

Future scopeof development

The formulation of a drug into various films has been popularin recent years. Several undesirable drawbacks associated with conventional dosage formssuch as inconvenience of administration, lower bioavailability andpatient non-compliance havepushed to the development of novel polymeric thin films as a drug delivery platform.This drug delivery platform is being under surveillance from both start-up and established pharmaceutical companies. The companiesstrive to design a wide range of thin films for oral, buccal, sublingual, ocularand transdermalroutes. Therefore, as an alternativeto conventionaldosage formspolymericthin films are expected to stand out as a dosage form to overcome the limitations posed by existingdosage forms. The film dosage form encounters several challenges during the phasesof formulation development and manufacture. Such issuesshould be addressed to optimize the overall formulation even after transferring to large scale manufacturing. The future looks very promising for the film technology in the time to comesas new technologies are rapidly introduced to prepare thin films.

II. CONCLUSION –

Fast dissolving films are intended to be applied in the mouth and it is a very innovative dosage especially to paediatric and geriatric patients. These dosage forms are of great importance in case of emergency conditions such as allergic reactions and asthmatic attacks where immediate onset of action of action is desired. Sublingual absorption is efficient since the percent of drug absorbed by this route is generally higher than that achieved by oral route. Therefore oral thin flims are an accepted technology for systemic delivery of API's.

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