E-ISSN: 2788-9270
P-ISSN: 2788-9262
NJPS 2021; 1(2): 49-56
Received: 12-05-2021
Accepted: 13-06-2021

Devendra Singh Lodhi
Associate Professor, Gyan Ganga Institute of Technology and Sciences, Bargi Hills Jabalpur, Madhya Pradesh, India

Aakash Singh Panwar
Institute of Pharmaceutical Sciences, SAGE University Indore, Madhya Pradesh, India

Pradeep Golani
Gyan Ganga Institute of Technology & Sciences, Bargi Hills Jabalpur, Madhya Pradesh, India

Megha Verma
Gyan Ganga Institute of Technology & Sciences, Bargi Hills Jabalpur, Madhya Pradesh, India

Correspondence
Devendra Singh Lodhi
Associate Professor, Gyan Ganga Institute of Technology and Sciences, Bargi Hills Jabalpur, Madhya Pradesh, India

A review of the combination of xanthine and bronchodilator drug in mouth-dissolving film for asthma treatment

Devendra Singh Lodhi, Aakash Singh Panwar, Pradeep Golani and Megha Verma

Abstract
There has been an increase in demand for caregiver dosage forms over the last two decades. In the oral cavity, mouth dissolving film (MDF) dissolves swiftly. Oral films that dissolve in your mouth function best when combined with medications that act quickly, such as Xanthine category drugs (Salbutamol Sulphate) and Xanthene Derivative Theophylline. According to the World Health Organization (WHO), asthma affects one in six adults and a quarter of all children, according to the World Health Organization (WHO). A child's admission to the hospital is often due to asthma, which is one of the most prevalent reasons for admission. During an asthma attack, quick-relief or rescue drugs are used to relax and open the airways, as well as ease symptoms. If prescribed, these medications can also be administered prior to exercise. To treat asthma, a combination of Salbutamol Sulfate and Theophylline is available in tablet form under the brand name "Theo-Asthalin." Oral films seem to be the most efficacious formulation. As a consequence, children with asthma should receive support from drugs given in the form of mouth-dissolving films, since they provide better patient compliance and an appropriate treatment method.

Keywords: Mouth dissolving oral film, theo asthalin, bronchodilators, xanthine, asthma

Introduction
About 60% of all formulations are in solid dosage form (i.e. pills). Tablets are the most popular dose type since they are easy to transport and administer. Many types of medications, such as peptides and proteins, cannot be taken orally because of hepatic decomposition and enzymatic breakdown in the gastrointestinal tract. Chewing gums are one of the suggested ways for systemic drug delivery, according to recent research. The buccal region of the oral mucosa is one of the hypothesised medication delivery channels. In addition, the gastrointestinal tract's enzyme flora is optimised for drug absorption by preventing hepatic first-pass metabolism. As early as the 1970s, a fast-dissolving drug delivery device [Figure 1.] when it comes to administering medications, the oral mucosa is a significant channel. One of the most common methods of developing bio adherent mucosal dosage forms is by using a polymer matrix. The buccal cavity is lined by a stratified squamous epithelium, which separates the lamina propria from the sub mucosa. However, buccal mucosa penetrability is four to four thousand times larger than intestinal mucosa. Chewing is an excellent way to absorb molecules that do not penetrate the skin well. Because of an uppermost layer of membrane-covering granules that produce intercellular objects, the oral mucosa is porous (200 m). A two to three-year shelf life can be expected for these oral film strips, depending on the active medicinal ingredient. In the past, patients who had difficulties swallowing tablets were given chewable tablets. Chewing also compromises the taste-masking qualities of the coating. Pre-dissolved in a glass of water, the soluble pills were administered to the patients, who then drank the solution. Taste masking, on the other hand, is more common than ever before. Taste masking, on the other hand, was more prominent than ever before. In addition, it was difficult to meet the requirement that all tablet components be water soluble [3].

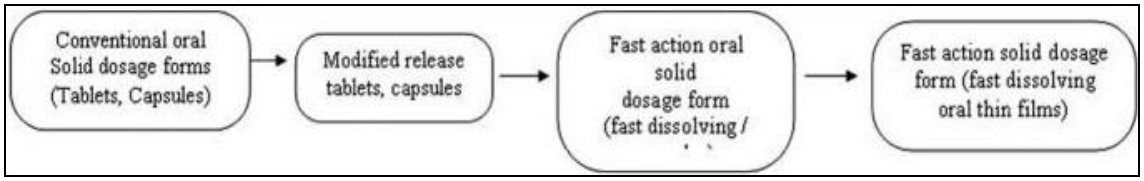

Fig 1: Stages in the development of oral solid dosage forms [1 Bala r *et al*. 2013] [1]

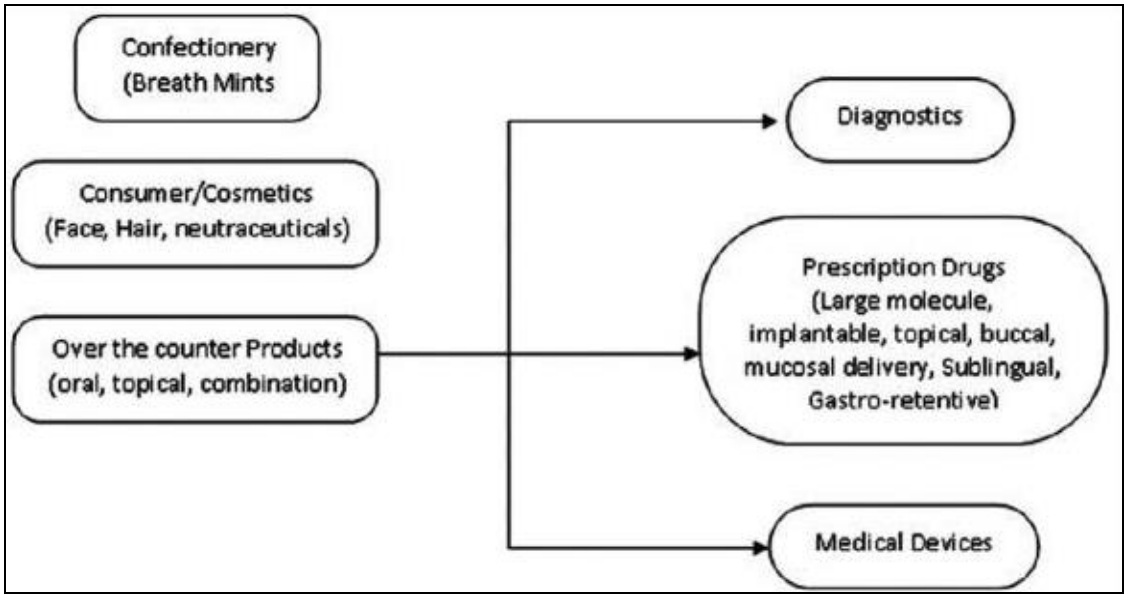

Fig 2: Stages in the development of oral solid dosage forms [1 Bala r *et al*. 2013] [1]

Description of the Oral Mucosa [Figure.3]

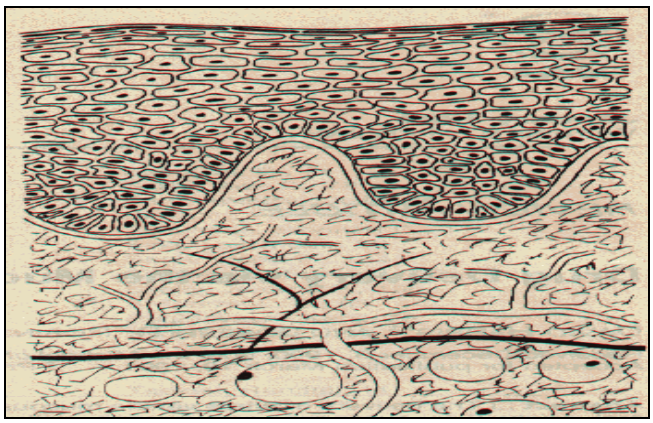

Fig 3: Structure of the oral mucosa

A. Structure [4, 5]

The uppermost layer of the oral mucosa is made up of a stratified squamous epithelium. The sub mucosa is the next inner membrane. Squamous stratified epithelium, which can be found all over the body, is comparable to the epithelium here. The epithelial cells expand in size and flatten as they travel from the basal layer to the superficial layer. Oral epithelial formation has been documented in 5-6 days. If you have a cavity, the oral mucosa will be thicker than normal. This mucosa is 500-800 microns thick, and the epithelium's makeup varies depending on where in the mouth you are. Triglycerides in the keratinized epithelium serve as a barrier. However, the non-keratinized epithelium lacks triglycerides, making it relatively impermeable. Small quantities of cholesterol, ceramides, and other polar lipids are also present. Evidence suggests that epithelial water permeability exceeds that of keratinized epithelium [5].

B. Permeable [6]

The oral mucosa is an epithelium with a small amount of leakage. The oral mucosa is 44000 times more permeable than the skin. Various oral mucosal architecture and functions contribute to differences in permeability. Clearly, the sublingual mucosa is more permeable than the cheek side or palate. Permeability barriers are believed to be the result of intercellular material developing in the oral mucosa and being coated with membranes (MCGs). During the separation process, MCG is generated and adheres to the cell's surface at the apical end of the cell's surface. Into the intercellular gap of the third epithelial layer, the protoplast sheath and contents are poured. Obstacles can be seen in plain sight on the surface layer. Horseradish peroxidises and lanthanum nitrate are used in penetration tests. When applied to the sub mucosal surface, permeation of cells is therefore hindered by cell layers with flat surfaces, while cells with bigger diameters have a reasonable ability to permeate. For prevention purposes, it turned out that keratinisation wasn't a good idea. In contrast, the non-keratinized epithelial MCG has a non-lamellar stack of lipids. Ceramides, sphingomyelin, and gluco chamber ceramide make up the MCG lipids of the keratinized epithelium. However, mucosal penetration is still constrained by the exterior epithelium, in addition to the basement membrane. The basal layer's composition isn't dense enough to remove big molecules [6].

C. Environment [7]

Mucus, a mixture of proteins and carbohydrates, surrounds oral epithelial cells in the mouth. Cells can move freely

because mucus acts as a lubricant and as a binding agent. Muscle adhesion may be facilitated by muco-adhesives, which are found in mucus. Mucus is present in the stratified squamous epithelium, but it is produced by goblet cells. Mucus saliva is the source of this substance. Most of the mucins in saliva are produced by the tiny salivary glands, which produce around 70% of all mucins. Because of the sialic acid and sulfurate residues in mucus, the mucus network has a negative charge, which plays a function in mucosal adhesion. Hard substances and chemicals can cause delicate tissues to rupture. An aqueous solution containing 1% organic and inorganic compounds. Among the most important salivary metrics is the rate of flow, which is affected by three factors: the time of day, the stimulus type and the intensity of the stimuli, respectively. 5.5 is the pH of saliva. Sodium and carbonic acid levels rise at high flow rates, and the pH rises. In order to hydrate the formulation, saliva is utilised in quantities of 0.5-2 L each day. As a result of oral mucosal water content, hydrophilic polymers are preferred as vehicles for oral mucosal drug delivery systems [7].

Absorption mechanism through the cheek mucosa [8]: Absorption mechanism through the cheek mucosa: Mucosal absorption through the cheeks two main penetration channels for passively delivering drugs exist [Figure no.4]. Penetrates can use any route, although depending on the drug's physicochemical qualities, one route is preferred over another. Due to the water-soluble nature of the intercellular cytoplasm, lipid medicines become less soluble. Cell membranes are lipidic, and hydrophilic substances have a low partition coefficient, which makes them difficult to flow through. The intercellular gaps become the primary barrier to lipophilic chemicals' penetration, whereas the cell membrane becomes the primary barrier to water-soluble compounds' transport. These two transport channels can be used in conjunction with each other to allow for solute penetration through the oral epithelium. A minimum roadblock, on the other hand, dominates the prevailing way [8].

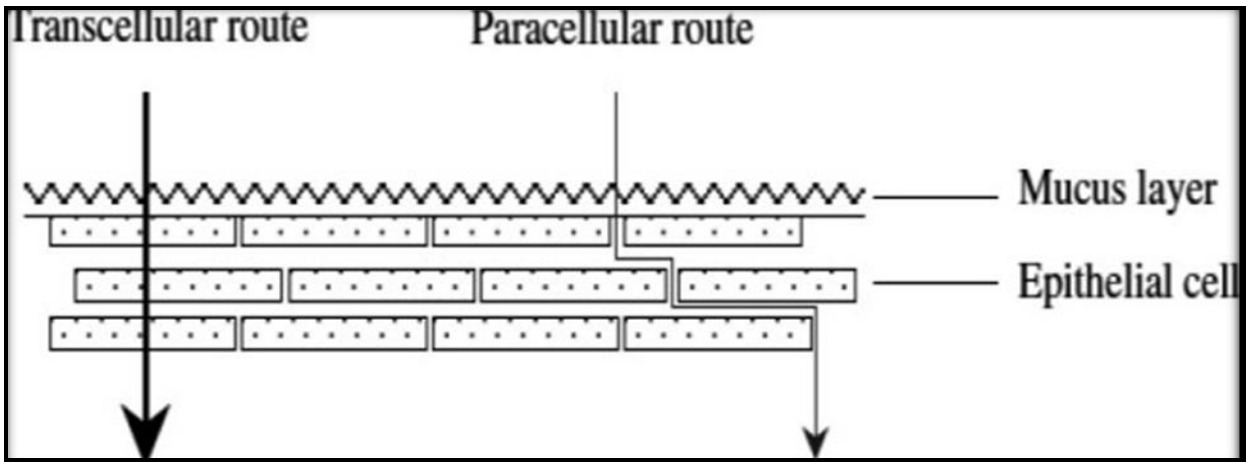

Fig 4: Pathways of drug absorption [Rathbone MJ *et al*. 2003] [3]

Fast Disolving Films [9, 10, 11]

A film that dissolves in the mouth is known as FDF (Fast Dissolving Film) or oral dispersion. This is a sort of oral medication delivery method. Transdermal patch technology was used in the development of this. It comprises of a thin film that is instantly moistened with saliva and placed on the patient's tongue, where it is absorbed. There is a lot of evaporation in this film. As a result, the medication is quickly released for absorption into the oral mucosa [4]. Because the film has a vast surface area, it disintegrates quickly when it comes into touch with a humid environment.

Definition of FDF: Film that dissolves quickly in your mouth is the most sophisticated solid dose form due to its flexibility.

In contrast to dissolving tablets, quickly dissolving APIs require less saliva to be effective in the oral cavity. Hydrophilic polymer dissolves fast in the tongue or cheek mucosa, delivering the medication to the bloodstream. To maximise bioavailability, the rapid drug delivery system uses a very low dose that will undergo multiple systemic metabolisms [9]. Features of speed films [10].

The film is thin and well designed.

- Available in various sizes and shapes.
- It doesn't get in the way.
- Easy to attach to the oral mucosa.
- Must go through quick disassembly.
- High-speed announcement.

Advantages of Fast Film [11]

- Proper dosing.
- No water required.
- Taste masking.
- Improved stability.
- Improved patient adaptability.
- The drug enters the systemic circulation, although the first-pass effect is small.
- Provide site-specific delivery and local measures.
- Large surface area availability that causes rapid buzzing and dissolution in the oral cavity.
- Dosage accuracy compared to syrup.

Fast Disolving Films Disadvantages [12]

- The disadvantage of FDS is that the strip cannot contain large volumes. The volume should be between 140 mg.

- When using filmstrip, the thickness in forming the film has technical drawbacks such as achieving dose uniformity.
- Packaging a film requires special equipment and is not easy to wrap.

Ideal Characteristics of Appropriate Drug Candidates [13]

- Drugs should be of a pleasant taste.
- Containing drugs should be used in low doses.
- The molecular weight of the drug should be medium.
- The drug should have good stability.
- The drug must be soluble in water and saliva.
- It must be fused to some extent at the pH of the oral cavity.
- Must have the ability to penetrate the oral mucosal tissue.

Oral Thin Film (OTF) Classification [14] [Table No.1]

Further classified into these three subtypes.

i). Flash emission.
ii). Mucoadhesive.
iii). Mucoadhesive sustained release wafers.

Table 1: Types of oral thin films with their properties [Rajni Bala *et al*. 2013] [1]

Properties	Flash release	Mucoadhesive melt-away wafers	Mucodhesive sustained released wafers
Area (cm^2)	2-8	2-7	2-4
Thickness (μm)	20-70	50-500	50-250
Structure	Single layer	Single or multilayer	Multilayer system
Excipients	Soluble hydrophilic polymers	Soluble hydrophilic polymers	Low/nonsoluble polymers
Drug phase	Solid solution	Solid solution or suspended drug particle	Suspension and/or solid solution
Application	Tongue (upper palate)	Gingival or buccal region	Gingival, (other region in the oral cavity)
Dissolution	60 s	In few minutes forming gel	Maximum 8-10 h
Site of action	Systemic or local	Systemic or local	Systemic or local

a) Freeze-drying system [15]

The system is the most popular in the world. Product approvals are the highest in the world. Using a mould or blister pack, a suspension or medication solution is combined with an excipient. A tablet-shaped unit is created. This is followed by lyophilization, which is the freezing of purification in packs and moulds. There is a high porosity in the resultant unit, which enables rapid dispersion of water or saliva at high speed. The active ingredient determines how well these systems regulate volume (water-soluble or insoluble drug). A number of taste-blocking substances can be included in tablets, which dissolve more quickly than syringes.

b) Compressed tablet-based system [16] compressed A conventional purification process is used to prepare the system. The hardness and crushing degree of the refining technique varies depending on the manufacturing method. To improve product protection and blister safety, the decomposition performance and packaging requirements are reduced to standard high density polyethylene (HDPE) bottles and package designs (such as those from CIMA Labs). It concludes with action. A water-soluble excipient or carbon-releasing or effervescent component is used in Bunhe's formulation to allow water to quickly infiltrate the purified core. Biovail Fuisz is an exception to this technology for purification. Using the shear form system, candy floss containing the medication is created. When combined with taste-hidden particles, the technology has the potential to integrate enormous quantities of psychoactive compounds. The main disadvantage is that it takes longer than thin or lyophilized formulations.

C) Tissue Film for Oral Use (OTF) [17]

If you've never heard the term oral wafer, it's a set of flat thin sheets of film that's taken orally. For many years, this type of film system has been used in the pharmaceutical industry, but it was just recently discovered in a new field. There have been soluble OTF or OS respiratory strips on the market for several years in confectionary and oral care items. Polymer coating companies with experience in developing APIs for transdermal drug

Table 2: Tissue Film for Oral Use

Properties	Lyophilized system	Compressed tablet based system	Oral thin films
Composition	Solution or suspension of drug with excipients	Active pharmaceutical ingredient with superdisintegrants	Hydrophilic polymers with drug and other excipients
Technology used	Lyophilization	Direct compression	Solvent casting, hot melt extrusion
Characteristics	High porosity which allow rapid water or saliva penetration and disintegration	Different levels of hardness and friability these result in varying disintegration and packaging needs	Large surface area leads to rapid disintegration
Packaging	Blister pack	High density polyethylene bottles	Blister cards with multiunits

Delivery is leveraging this OTF technology. Fast-dissolving technology classification [Rajni Bala *et al*., 2013] [1] Formalized, OTF is a proven and accepted technology that transmits drugs systemically. OTC drugs are in the early to mid-term development stage of prescription drugs [Table No.2].

Composition standard of oral-acting strips Dissolving film for oral consumption [18]

API is contained in a thin, flat film with a surface area of 120 cm2 (depending on dose and drug load). There is no limit to how much medicine can be put into a single dose. Most of the effects of mechanical characteristics of the film are attributed to formulation considerations (plasticizer polymer, etc.).Table No.3]

Table 3: Standard composition of fast dissolving films [Deshmane SV *et al*. 2011 [18]

Ingredients	Amount	Examples
Drug	5-30%w/w	Antiallergic, antiemetic, antiepileptic, antimigrant
Water soluble polymer	45%w/w	HPMC E3, E5 and E15 and K-3, Methyl cellulose A-3, A-6 and A-15, Pullulan, carboxmethylcellulose cekol 30, polyvinylpyrollidone PVP K-90, pectin, gelatin, sodium, alginate, hdroxypropylcellulose, polyvinyl alcohol, maltodextrins
Plastisizers	0-20%w/w	Glycerol, dibutyl pthallate, polyethylene glycol, etc.,
Surfactants	q.s.	Sodium lauryl sulfate, benzalkonium chloride, Tween, etc.,
Sweetening agents	3-6%w/w	Saccharin, cyclamate, and aspartame
Saliva stimulating agents	2-6%w/w	Citric acid, malic acid, lactic acid, and ascorbic acid
Fillers, colors, flavors	q.s.	FD and C colors, US FDA approved flavors

HPMC: Hydroxypropyl methylcellulose, US FDA: United states food and drug administration, q.s.: Quantum satis

Formularity [19] Formulation of solvents Water-soluble polymers are dispersed in water at a high speed of 1,000 rpm and heated to 60 °C in this process. Colors, flavours, and sweeteners are dissolved in a separate cup. A high-speed (1000 rpm) mixer was then used to mix the above solutions together. In a suitable solvent, the resultant solution is combined with the prelocular API. In a vacuum, the bubbles are squandered. It is then selected in the film and allowed to dry, after which the film is cut into the desired size pieces.

The hot melt extrusion [20, 21]

To begin, the operator was used to create a starting volume of material. Drugs are mixed with the shrubs and solid volume to create an initial volume before being dried. After that, the dried granular material is placed in the extruder for further processing. There are four different temperatures on an extruder: surface 1 (800 ° C), surface 2 (1150 ° C), surface 3 (1000 ° C), and surface 4 (650 ° C). Extruder screw speed must be set to 15 rpm in order to melt the mass correctly in 34 minutes. 650 °C extrusion into cylindrical cylinders forms thin film by pressing the extrusion.

A half-resistance time [22, 23] spell Insoluble polymeric acid is employed in electrical formulae when this approach is applied. As a result of this process, dissolved polymers are dissolved in local water. This solution was then added to the acidic polymer solution to create a new solution. Plasticizers were added after a proper mixing of two-soluble solutions to create a gel mass. Finally, the gel volume is put into the drum with the temperature protected by a thermometer. Then, the two solutions are carefully blended together. There must be a tolerance of 0.01510.051 in the width of the produced film.

Distributions [24] are fixed. In this approach, the medication is dispersed in a liquid polymer solution. For solid dispersion, oral medicine is dispersed in a solvent and the resulting solution is then added to melting the appropriate polymer at temperatures below 70°C without removing any liquid solvent. Last but not least, a dye-fixed dispersion was transferred to the nitrate-based film.

Methods for rolling [25, 26, 27] How to roll As a result of the rolling approach, both polymer and medication solutions are continually combined before being subjected to rollers. There must be a particular viscosity in the solution. There are several ways to trim and shape the film when it dries.

Patent-protected approach [28, 29]

In this film, you'll find a wide range of pharmaceuticals and health products. As the name implies, it's a vegetarian dish. With its official transformation and nonstop production mechanism removed, the film has a more open production environment. Movies In addition to facial covering and colouring, Gels TM can be used with pharmaceuticals. Different water-soluble polymers, which are carefully optimised for application purposes, are used to create this form of film.

Solulaser [30]

Solulaser Oral delivery films containing active ingredients, colours, and fragrances are produced using this method. When stored on the tongue, the Solulaser TM membrane is engineered to disintegrate fast, releasing the active and taste components quickly. As a result of these properties, these films are palatable and transport medications quickly to the mouth. Soluleave TM tablets or capsules can also be made to adhere to the mucous membrane and release active ingredients over a period of more than 15 minutes, making this governance regime ideal for persons with patients or elderly age difficulties.

Wa Ftab [31]

In a well-equipped filmstrip, this is a pharmaceutical distribution system. If you're using Wafer Tab, the wavy saliva area enables quick dissolution and release of active components. WaFtab TM is a film strip that can be flavoured to improve flavour masking. In the XGEL TM Musiced film, the dose of the active component is precisely fixed and protected from heat and moisture, resulting in a more stable dosage. Can be produced in a number of forms and sizes, making it ideal for patients who have difficulty swallowing medications that require quick release.

Foam burst [32]

To create this internal gas flow during the film-making process. When the honeycomb structure is broken down, a new emotion is left behind. As a result, Foamburst TM has grabbed the attention of confectioners and food producer's alike. Aims to merge specific micro technologies and films in 2004 with MICP MICAP SPS. For the notice to cease smoking, the development seeks to give novel pharmaceutical supply systems for the notification [32].

Asthma [33]

When the airways of the lungs inflame and expand, it becomes difficult to breathe and air can't enter or exit the lungs. For example, people with allergies or an ancestry of asthma are more prone to developing it. Allergies are often to blame for asthma. An example of this would be allergic asthma. There's a condition called occupational asthma that occurs when a worker inhales toxic fumes or gases or powders at work. Asthma affects a large number of children

and families. Asthma affects a large number of children under the age of 5.Exercise-induced asthma (EIA): This patient develops asthma due to physical activity. And other healthy people suffer from asthma while exercising. This is called exercise-induced asthma (EIA).

Cause [34]

Asthma's cause is still a mystery. Factors that contribute to asthma include: Early childhood antibiotic use; the number and duration of respiratory infections during this time period; genetic variables. Occupational exposure to dust and chemicals in most asthmatics, the airways are irritated to some degree. Additionally, their prayers are based on triggers, or specific situations. When an already enlarged prayer contracts, it can cause an asthma attack. Asthma triggers vary from person to person.

Common asthma triggers include

- Pollen
- Dust
- Animals
- Air Pollution
- Food Additives
- Strong Perfume
- Exercise
- Tobacco Smoke
- Some Medicines Example: Aspirin
- Respiratory Infections
- Temperature Changes and Humidity
- Psychological Effects Example: Extreme emotions
- Irritation at work Examples: paint smoke, flour, wood floor.

Signs and Symptoms Common signs and symptoms of asthma include: [35]

- Cough - likely to get worse at night
- Shortness of breath
- Chest stricture
- Shortness of breath
- Unspeakable (in very severe seizures)
- Blue around mouth (in very severe seizures) Administration

Asthma is not curable, but it can be treated with drugs that are taken away from the triggers that cause it to flare. Asthma treatments are widely available. Consultants discuss which drugs are best for a certain individual patient. Asthma is typically treated with the following types of medications: Anti-inducers: Anti-inducers are inhaled corticosteroids that assist lower stress and diminish the body's sensitivity to inducers in general. Asthma episodes can be prevented by taking it on a daily basis. As an example, Flixotide, Pulmicort and Beclozone. Resting the prayer muscles relieves tension and helps prevent asthma. The term bronchodilators are often used to describe them. Taking the palliative before a common instigator (exercise) is recommended. Bricanyl and Ventolin are two examples. An inhalation palliative given with prophylactics. Two doses every day help to keep the prayer muscles relaxed. Foradil and Serevent, for example. Combined Inhaler: The combined inhaler combines preventative agents and symptomatology control into one device. Examples are Seretide and Symbicort. Inflation is necessary for the above medications to reach the lungs, where they instantly begin to work. Patients with frequent and/or severe asthma symptoms may need periodic treatment/therapy adjustments, as well as higher medicine dosages. It may be necessary to administer corticosteroid medication in liquid or tablet form until the symptoms have subsided or disappeared. The symptoms of severe asthma attacks must be treated immediately in the hospital. An oxygen nebulizer or intravenous infusion is used to treat seizures (injecting into water droplets on the hands or arms).

Health-Related Aspects [36]

A bioequivalence study was conducted between an oral disintegrating tablet formulation and an oral dissolving film formulation (ODF). Develop oral film products if you wish. The new clinical study has the advantage of giving the product a three-year commercial exclusivity period. According to the European Medicines Agency's instructions, marketing authorization clearance is required in Europe. Either a phase-by-phase approach or a mutual approval process is possible. In Japan, product approval is handled by the Ministry of Health, Labour, and Welfare. It's important to note that most of the regulation is centred on taste and palatability, especially for products meant for children. These tests are carried out on both animals and humans. As for animal research, the hamster ball pocket is the most suited model. It's a trustworthy model that can anticipate stimulus requirements before it's used on humans. Clinical endpoints play a crucial role in clinical research. Primary and secondary results must be measured. To show the superiority and benefits of the newly designed OS over existing formulations. Guidelines for product development have been developed by the ICH. Pharmacists have the option of developing drugs in accordance with the Q8 standards from the International Conference on Harmonization (ICH). The aims of clinical research procedures must be well defined. Another aspect will be addressed in a separate research study. Study plans must be sufficiently detailed (with supporting reasons) to comprehend major health risks. For example, soft tissue and/or hard tissue effects are taken into account when calculating the size of a study's sample size. All endpoints must be specified. Use patterns (single or many applications) are described in this section. Describe the time of follow-up after the therapy (for example, a single application with a follow-up period of 1, 3, 6, or 12 months, multiple applications with a longer follow-up period, etc.) As well as a summary of the theme sources, selection criteria, and techniques, it should also provide relevant analytical information.

Combined Therapy [37, 38, 39, 40]

Combined Therapy for Asthma treatment relies on a combination of therapies. Xanthenes Category medications and bronchi’s have been shown to be effective in several trials. Due to the fact that it improves asthma control, and the recommendations recommend it as the optimum therapy for individuals with moderate to severe asthma, this is the case. Doctors can treat both inflammation and bronchoconstriction of asthma using combination treatment, which involves the use of and Xanthine in an oral film. Combining Xanthine and Bronchodilator in one device is an important step forward in the treatment of asthma, given the ability to adjust the dosage of inhaled corticosteroids (ICS). The complexity of therapy must be reduced, especially for

patients who require several therapies, and patient compliance must be improved. If you're worried about medication penetration into the airways and not treating the systemic component of your asthma, mouth dissolving treatment may be able to help you with that as well. When used at low therapeutic dosages, the inhaled formulation does have a small number of adverse effects for both children and adults. Xanthine, according to current research, has no major side effects when taken in the therapeutic region. In certain research, the safety of Bronchodilator has been called into doubt. As a result, regular therapy with this class of drugs isn't necessary, but it should be combined with inhalation since it increases the risk of mortality and worsening of severe disease in this patient group of people. Steroids even while asthma-related fatalities have not increased since the introduction of Xanthenes into clinical practise, according to its maker, they have actually decreased. It was also observed that in one-third of asthmatics and in half of cases with symptoms increasing, inadequate nutrition was to blame.

Conclusions

When combined with Bronchodilator as an MDF, Xanthine and Bronchodilator might effectively treat the bronchoconstriction component of asthma without the need for additional complimentary and synergistic adjustable maintenance dose forms. That's what I was able to do. The use of a film that dissolves in the mouth has been shown to be beneficial in treating acute asthma episodes, according to new research. In addition, new concepts are used as both a maintenance treatment and a relaxation therapy for asthma sufferers since they are proven to be safer and more successful than set dosage. Also, children as young as 4 years old may now be treated comfortably on the combo therapy unit. Additionally, the Combination Device lowers the complexity of treatment, allowing for a more personalised approach to asthma management. For clinicians, this technique looks perfect, as it represents one of the most significant breakthroughs in modern asthma therapy. Building collaborative connections between patients and healthcare providers cannot be overemphasised. Its goal is to empower patients to take charge of their health.

References

1. Bala R, Pawar P, Khanna S, Arora S. Orally dissolving strips: A new approach to oral drug delivery system. Int J Pharm 2013;3(2):67-76.
2. Shojaei A. Buccal Mucosa as A Route for Systemic Drug Delivery: A Review. J Pharm Pharm Sci 1998;1(1):15-30.
3. Rathbone MJ, Hadgraft J, Roberts MS. Modified – release drug delivery technology, Marcel Dekkar 2003;1:203-204.
4. Dixit RP, Puthli SP. Oral strip technology: Overview and future potential, Journal of Controlled Release 2009;139:94-107.
5. Radhakishan UR. Mouth dissolving film and their patent: An Overview, IRJP 2012;3(9):39.
6. Eixarch H. Drug Delivery to the Lung: Permeability and Physicochemical Characteristics of Drugs as the Basis for a Pulmonary Biopharmaceutical Classification System (pBCS). Journal of Epithelial Biology & Pharmacology 2010;3:1-14.
7. Prasanthi NL. Design and Development of Sublingual Fast Dissolving Films for an Antiasthmatic Drug. Der Pharmacia Lettre 2011;3(1):382-395.
8. Shyu WC, Mayol RF, Pfeffer M, Pittman KA, Gammans RE, Barbhaiya RH. Biopharmaceutical evaluation of transnasal, sublingual and buccal disk dosage forms of butorphanol. Biopharm Drug Dispos. 1993; 14:371–9 1996;48:1256-59.
9. Brakemeier EL, Radtke M, Engel V, Zimmermann J, Tuschen-Caffier B, Hautzinger M, *et al*. Overcoming Treatment Resistance in Chronic Depression: A Pilot Study on Outcome and Feasibility of the Cognitive Behavioral Analysis System of Psychotherapy as an Inpatient Treatment Program. Psychother. Psychosom 2014;84:51–56.
10. Patel R, Prajapati S, Raval A. Fast dissolving films (FDFs) as a newer venture in fast dissolving dosage forms, Int J Drug Dev& Res 2010;2(2):232-236.
11. Rathi, V, Senthil V, Kammili L, Hans R. A brief review on oral film technology, Int J Res Ayurvedic & Pharmacy 2011;2(4):1138-1147.
12. Kathe, Kashmira; Kathpalia, Harsha Asian Journal of Pharmaceutical Sciences, Volume 12, Number 2017;6:487-497(11)
13. Singh R, *et al*. Chem. Res. Toxicol 2003;16:198.
14. Hussain MW, Kushwaha P, Rahman MA, Akhtar J. Development and Evaluation of Fast Dissolving Film for Oro-Buccal Drug Delivery of Chlorpromazine. Indian Journal of Pharmaceutical Education and Research 2017;51:S539–S547
15. Universidade Federal do Rio Grande do Norte *et al*. Freeze-drying of emulsified systems: A review Volume 503, Issues 1–2, 30 April 2016, 102-114.
16. Keerthi ML, Kiran RS, Rao VUM, Sannapu A, Dutt AG, *et al*. Pharmaceutical Mini-Tablets, its Advantages, Formulation Possibilities and General Evaluation Aspects: A Review. Int. J Pharm. Sci. Rev. Res 2014;28:214-221
17. Macedo AS, *et al*. Novel and revisited approaches in nanoparticle systems for buccal drug delivery. J Control. Release 2020;320:125-141.
18. Dash V, Kesari A. Role of Biopharmaceutical Classification System in Drug Development Program. JCPR 2011;5(1):28-31.
19. Qadir AK. Formulation and evaluation of fast dissolving films of loratidine for sublingual use, IRJP 2012;3(7):157-161.
20. El-Egakey MA, Soliva M, Speiser P. Hot extruded dosage forms. Technology and dissolution kinetics of polymeric matrices. Pharm Acta Helv 1971;46(1):31-52.
21. McGinity JW, Zhang F, Koleng J, Repka M. Hot-melt extrusion as a pharmaceutical process. Am Pharm Rev 2001;4:25-37.
22. Jain K, Awasthi S, Kumar P, Somashekariah BV, Phani AR. Formulation and Pharmacokinetic Studies of Rapidly Dissolving Nanofibers. Middle-East J Sci Res 2014;22(8):1176 -80
23. Bera A, Mukherjee A. A Detailed Study of Mouth Dissolving Drug Delivery System. Acta Chim Pharm Indica 2013;3(1):65-93
24. Chaudhary H, Gauri S, Rathee P, Kumar V. Development and optimization of fast dissolving oro-dispersible films of granisetron HCl using Box–

Behnken statistical design. Bull Fac Pharm, Cairo Univ 2013;51(2):193-201
25. Mishra DN, Bindal M, Singh SK, Vijaya Kumar SG. Spray dried excipient base: a novel technique for the formulation of orally disintegrating tablets. Chem Pharm Bull (Tokyo) 2006;54(1):99-102.
26. Mangal-Mohit TN, Bansal R, Thakral S, Goswami M. Fast dissolving tablet: an approach for emergency treatment. Int J Res Ayurveda Pharm 2012;3(3):377-80.
27. Dokala GK, Pallavi C. Direct compression-an overview. Intl J Res Pharm Biom Sci 2013;4(1):155-8.
28. Shiv G, Ajay P, Prateek P, Sanket T, Deepu P, Pramod S *et al*. Formulation and Evaluation of Fast Dissolving Tablet of Ziprasidone HCL. Am J Pharm Res 2013;3(4).
29. Bhattarai M, Gupta A. Fast Dissolving Oral Films: A Novel Trend to Oral Drug Delivery System. Sunsari Technical College Journal 2015;2(1):58-68.
30. Usha Kiran Reddy T, Sunil Kumar Reddy K, Katta Manogna, Thyagaraju K. A Detailed Review on Fast Dissolving Oral Films. Indo American Journal of Pharmaceutical Research 2018;8(06).
31. Sanna Ghodake P, Kailas Karande, Riyaz Ali Osmani, Rohit R. Bhosale, Bhargav R. Harkare, Birudev B. Kale, Mouth Dissolving Films: Innovative Vehicle for Oral Drug Delivery. International Journal of Pharma Research and Review 2013;2(10):41-47.
32. Chaurasiya P, Kharel R, Manasa DR, Rajashekhar V, Sridhar KA. A Review on Oral Fast Dissolving Films A Novel Drug Delivery System, Asian Journal of Research in Chemistry and Pharmaceutical Sciences 2016;4(4):165-175.
33. Joshua JM, Hari R, Jyothish FK, Surendra SA. Fast Dissolving Oral Thin Films: An Effective Dosage Form for Quick Releases. International Journal of Pharmaceutical Sciences Review and Research 2016;38(1):282-289.
34. Padamwar PA. Formulation and Evaluation of Fast Dissolving Oral Film of Bisoprolol Fumarate. International Journal of Pharma Sciences and Research 2015;6(1):135-142
35. George SJ, Vasudevan DT. Studies on The Preparation, Characterization, and Solubility of 2 HP-β-Cyclodextrin-Meclizine HCl Inclusion Complexeses. Journal of Young Pharmacists 2012;4(4):220-227.
36. Ali MS, Vijendar C, Sudheerkumar D, Krishnaveni J. Formulation and Evaluation of Fast Dissolving Oral Films of Diazepam, Journal of Pharmacovigilance 2016;4(3):1-5.
37. Lee J, McDonald C. Review: Immunotherapy improves some symptoms and reduces long-term medication use in mild to moderate asthma. Annals of internal medicine 2018 Aug 21
38. Tesfaye ZT, Gebreselase NT, Horsa BA. Appropriateness of chronic asthma management and medication adherence in patients visiting ambulatory clinic of Gondar University Hospital: a cross-sectional study. The World Allergy Organization journal 2018.
39. Piloni D, Tirelli C, Domenica RD, Conio V, Grosso A, Ronzoni V *et al*. Asthma-like symptoms: is it always a pulmonary issue? Multidisciplinary respiratory medicine 2018.
40. Rajan S, Gogtay NJ, Konwar M, Thatte UM. The global initiative for asthma guidelines (2019): change in the recommendation for the management of mild asthma based on the SYGMA-2 trial - A critical appraisal. Lung India: official organ of Indian Chest Society 2020.
41. National Asthma Education and Prevention Program. Guideline for the diagnosis and management of asthma. Expert Panel Report II. Bethesda (Md); NIH, National Heart, Lung, and Blood Institute, 1997, NIH publication 097-4051.
42. Janson C, Chinn S, Jarvis D *et al*. Physician-diagnosed asthma and drug utilization in the European Community Respiratory Health Survey. Eur Respir J 1997;10:17951802.
43. Magnus P, Jaakkola JK. Secular trend in the occurrence of asthma among children and young adults: critical appraisal of repeated cross sectional surveys. BMJ 1997;314:17951799.
44. Weinberg EG. Urbanization and childhood asthma: an African perspective. J Allergy Clin Immunol 2000; 105: 224-231 5. Saleh JA, Ind PW. Concurrent therapy (long acting beta agonists and inhaled corticosteroids) in the management of asthma. Nig J Med 2006;15(4):359-363.