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Review of Formulation and evaluation of mouth disolving film by using Nimesulide

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ABSTRACT:
Mouth dissolving film is the most advanced oral solid dosage form due to its flexibility and comfort in use. Mouth dissolving films are oral solid dosage form that disintegrate and dissolve within a minute when placed in mouth without taking water or chewing. This dosage form allows the medication to bypass the first pass metabolism so bioavailability of medication may be improved .Mouth dissolving film has potential to improve onset of action lower the dosing and eliminate the fear of chocking. Formulation of mouth dissolving films involves both the visual and performance characteristics as plasticized hydrocolloids, API taste masking agents are being laminated by solvent casting and semisolid casting method. Solvent casting method being the most preferred method over other methods because it offers great uniformity of thickness and films prepared having fine glossy look and better physical properties. Mouth dissolving films are evaluated for its various parameters like thickness, physical property like folding endurance, disintegration and dissolution time. This review gives an idea about formulation techniques, evaluation parameters, overview on packaging and some available marketed products of mouth dissolving films.
Keywords: Mouth dissolving film, solvent casting, fast disintegration.

I. INTRODUCTION:

Fast Drug Delivery Systems are rapidly gaining interest in the pharmaceutical industry. These systems either dissolve or disintegrate generally within a minute without needing water or chewing. These systems offer superior clinical profiles with potentionaloro mucosal absorption thus increasing the drug bioavailability with respect to oral administration. Recently thin films have been proposed which rapidly dissolves or disintegrates into buccal cavity. Mouth dissolving films are novel dosage forms that disintegrate or dissolve in the oral cavity. These are ultra thin postage stamp size with an active agent or pharmaceutical excipients. These dosage forms are placed on the tongue or any mucosal tissue. When wet with saliva, the films rapidly hydrates and adheres on to the site of application. It rapidly dissolves or disintegrates to release the medicine for mucosal absorption or with modification, allows for oral GIT absorption with quick dissolving properties.

An important benefit of these dosage forms is accurate dosing as compared to liquid dosage form, no water is needed and there is no fear of choking as compared to tablets and capsules. After disintegrating in the mouth, enhanced the clinical effect of drug through pre-gastric absorption from mouth pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form. More recently, Fast-dissolving buccal film drug delivery systems have rapidly gained acceptance as an important new way of administering drugs. They are usually used for pharmaceutical and nutraceuticals products. It is the newest frontier in drug delivery technology that provides a very convenient means of taking medications and supplements. Fast dissolving films are also applicable when local action in the mouth is desirable such as local anesthetic for toothaches, oral ulcers, cold sores, orteething Oral route is the most preferred route of administration for systemic effect. About 60% of all formulations are of solid dosage form. Tablet is the most preferred dosage form due to ease of transportation, manufacturing and more patient compliance. Generally pediatric geriatric and forbidden patients experience difficulties in swallowing the conventional tablet. To overcome this problem a novel formulation was developed .i.e. oral fast dissolving films (Siddiquinehal et al., 2011) . FDF is prepared using hydrophilic polymers that rapidly dissolves on the tongue or buccal cavity, delivering the drug to the systemic

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circulation via buccal mucosa. (Mahajan AN et al.,2011). The fast dissolving drug delivery system are specially designed for the drugs which have extensive first pass metabolism and have low dose, for the enhancement of bioavailability. (Suresh B 2006).

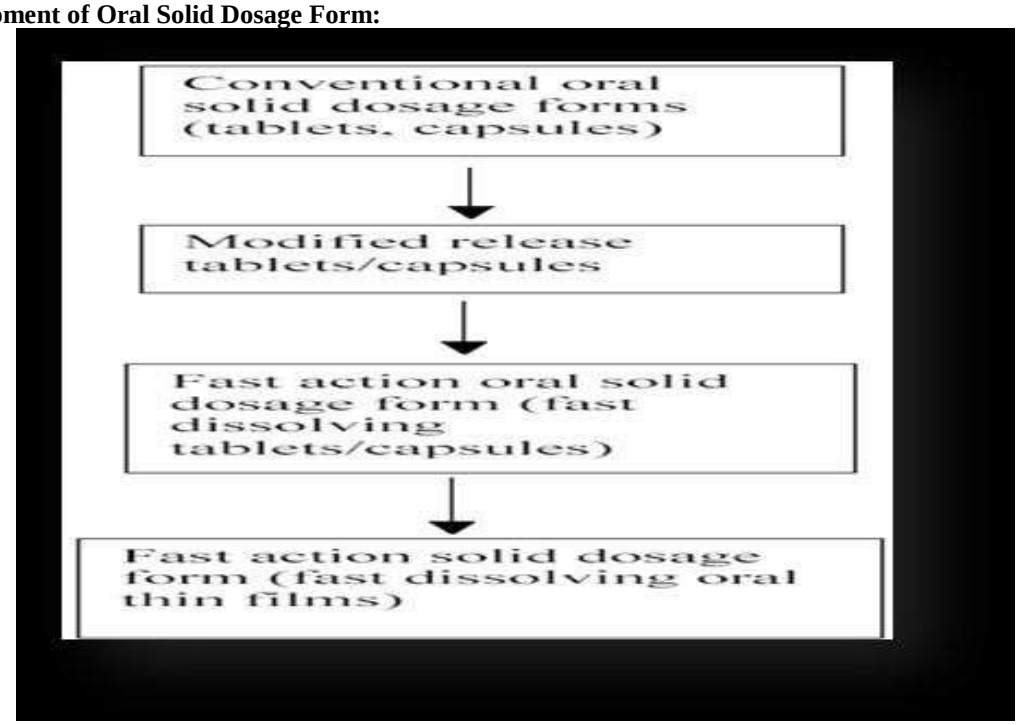
Special features of mouth dissolving films:
• Thin elegantfilm
• Available in various size andshapes
• Unobstructive
• Excellentmucoadhesion
• Fastdisintegration
• Rapidrelease

Advantages:
• Convenient dosing
• No waterneeded
• No risk ofchocking
• Tastemasking
• Enhanced stability
• Improved patientcompliance

Disadvantage:
It is hygroscopic in ngure so it must be kept in dryplaces. o Packaging of films requiresspecial equipment's and it is difficult topack. o High dose cannot be incorporated into theoral film. o Eating and drinking may become restricted. o Mouth dissolving film aremoisturesensitive**.**

Ideal Requirements:
The ideal requirements for ODF are summarized below 7-9 :
• ODF should be thin and flexible, but stable to guarantee a robust manufacturing and packaging process and ease of handling andadministration.
• The films should be transportable, not tacky and keep a plane form without rollingup.
• Ease of administration for patients who are mentally ill disabled anduncooperative.
• They should provide an acceptable taste and a pleasantmouth-feel.
• Require no water. • Disintegration time should be as short aspossible.
• They should exhibit low sensitivity to environmental conditions such as temperature andhumidity.
• They should have ability to provide advantages of liquid medication in the form of solid preparation.
• Size of a unit FDF should not be too large that it will affect the patient'scompliance.
• Surface of the FDF should be smooth anduniform.
• They should remain physically and chemically stable throughout its shelflife.
• Cost effective and ease of commercial production.

Development of Oral Solid Dosage Form:



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Composition Of Mouth Dissolving Film:

Composition	Concentration
Drug	1-25%
Watersolublepolymer	40-50%
Plasticizers	0-20%
Fillers,colors,flavors	0-40%

II. LITERATURE REVIEW:

1. Nihar Shah (2015), Sublingual route is a useful when rapidonset of action is desired with better patient compliance. The portion of drug absorbed through the sublingual blood vessels bypasses the hepatic first pass metabolism processes giving acceptable bioavailability. Fast dissolving drug delivery is rapidly gaining acceptance as an important new drug delivery technology, which aim to enhance safety and efficacy of a drug molecule to achieve better patientcompliance.

2. Mandeep Kaur (2011), Orally fast dissolving films (OFDFs) have been introduced in the market recently as they provide convenience and ease of use over other dosage forms such as orally disintegrating tablets. 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 OFDFs are gaining the interest of large number of pharmaceutical industries. Orally fast dissolving film 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. OFDFs are very similar to postage stamp in their shape, size andthickness.

3. Shivani B. Sontakke Patil (2020), Current innovations have introduced suitable measurement choices from the oral course for pediatrics, geriatric, abnormal, nauseous or turbulent patients. Fast dissolving mouth Film is formulated utilizing hydrophilic polymers that quickly disintegrate on the tongue or buccal pit, conveying the medication to the systemic circulation through disintegration when contact with the fluid is made. Hydrophilic polymers are utilized as film formers for quick dissolving films. The water-soluble polymers accomplish quick dissolution, great mouth feel, and mechanical properties to the films. Quick dissolving oral thin film offers quick, exact dosing in a safe, effectual format that is advantageous and convenient, without the requirement for water or estimatinggadgets.

4. Dr. Rakesh Gupta (2017), These films generally dissolve within seconds to release the active agents but can be modified to release the drug more slowly depending upon film thickness and selection of the polymer matrix. A film or strip can be defined as a dosage form that employs a water dissolving polymer which allows the dosage form to quickly hydrate, adhere and dissolve when placed on the tongue or in the oral cavity to provide rapid local or systemic drug delivery. Upon complete disintegration, absorption of the API may occur through the buccal mucosa. Esophageal absorption may also occur during the process of swallowing saliva that contains the dissolved API. The majority of the dose ultimately ends up in the stomach and is absorbed in the GI tract in a similar manner as a traditional tablet. A traditional oral dosage form requires a fixed amount of time for stomach fluids to dissolve the entire tablet orcapsule.

5. ShahnawazAnis (2011), There has been increased demand for the novel dosage forms to gain more patient compliance. Mouth dissolving dosage forms are gaining popularity in recent times, as these dosage forms requires no water for administration. Rofecoxib, a NSAID widely used in the management of osteoarthritis and dental pain. Being water insoluble drug, the onset of absorption and pharmacological action depends mainly on its dissolution. The aim of the present work was to formulate and evaluate mouth-dissolving film containing Rofecoxib. Films were formulated using HPMC-15cps and polyvinyl alcohol as two different film- forming agents. Rofecoxib was dispersed in the polymer solution. Films were prepared by casting method and found to satisfy the mouth dissolving time and other film parameters. Film instantly get wet by saliva, rapidly hydrates, adheres to tongue and rapidly disintegratesand dissolves to release the drug for the oral mucosal absorption or allow for gastrointestinal
absorption to be achieved when swallowed. The formulated films exhibited acceptable film endurance. Time required for the film to dissolve and release the drug was found to be 30 seconds and 1 minute respectively.

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6. Syed Naiem Raza (2016), The objective of the present study was to develop mouth dissolving films (MDF) of Losartan potassium for the treatment of hypertension, with fast disintegration, optimum morphological properties, and mechanical strength. Losartan is an anti-hypertensive drug which undergoes extensive first-pass metabolism that results in low bioavailability of the drug. Through buccal route, the drug directly enters blood circulation and hence bioavailability of the drug increases. Hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, sodium alginate, and gelatin were used as the hydrophilic film-forming polymeric bases and glycerol as plasticizer. Films were prepared by solvent casting technique. Parameters like in- vitro disintegration time, tensile strength, content uniformity, folding endurance, swelling index, and in-vitro drug release wereevaluated.

7. PawarRajat (2019), Mouth dissolving film is the most advanced oral solid dosage form due to its flexibility and comfort in use. Mouth dissolving films are oral solid dosage form that disintegrate and dissolve within a minute when placed in mouth without taking water or chewing. This dosage form allows the medication to bypass the first pass metabolism so bioavailability of medication may be improved .Mouth dissolving film has potential to improve onset of action lower the dosing and eliminate the fear of chocking. Formulation of mouth dissolving films involves both the visual and performance characteristics as plasticized hydrocolloids, API taste masking agents are being laminated by solvent casting and semisolid castingmethod.

8. Dr. K. R. Biyani (2020), Oral route is considered as one of the most convenient route for administration of various pharmaceutical dosage forms like, tablet, capsule, syrup, suspension and emulsion. Fast Dissolving Drug Delivery systems have developed various fast disintegrating preparations like mouth dissolving film, MDT. Oral thin film are new dosage form that are prepared from hydrophilic polymer which are when placed in mouth, buccal cavity disintegrate rapidly. Mouth dissolving film is superior as compare to mouth dissolving tablet as the cost of production is low. Geriatric and pediatric patients are facing difficulty in swallowing of tablet and capsule, the oral film can bypass it, along with that it has other advantages like self-administrable, fast dissolving, rapid absorption that make it versatile dosageform

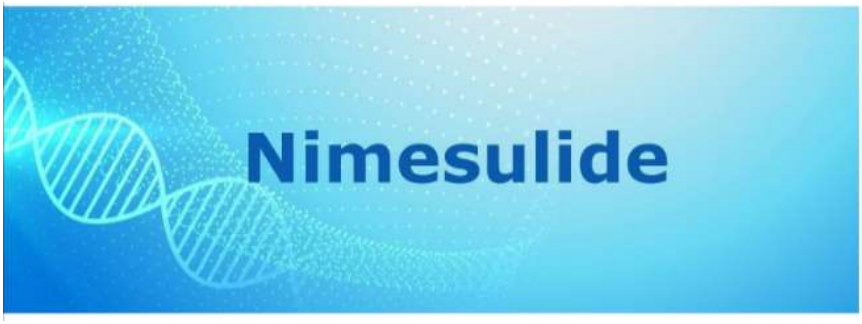
Drug (Active Pharmaceutical Ingredient):

• Different type of API can be successfully incorporated in the Mouth dissolvingfilm.
• Micronized API can improve the texture of the film and also dissolution and uniformity of the oral fast dissolvingfilm.
• Taste of bitter drug need to be masked for that cyclodextrins or resins can be used; they prevent the direct contact of API with thesaliva.
• The dug should have high solubility and high permeability (BCS class1).
• The drug should have lowdose

• Itincludes

➢ Cough/Cold Remedies (antitussive, Expectorants)- AmbroxolHCL.
➢ CVS Agent- Valsartan,Verapamil..
➢ Antihistamines- Levocetrizine HCL.,
➢ Antiasthamatics- Salbutamol sulphate, Montelukastsodium.
➢ Nausea-Domperidone,
➢ Pain NSAIDS/Paracetamol Tramadol JhumrofenNimesulide

Drug & Excipient Profile:



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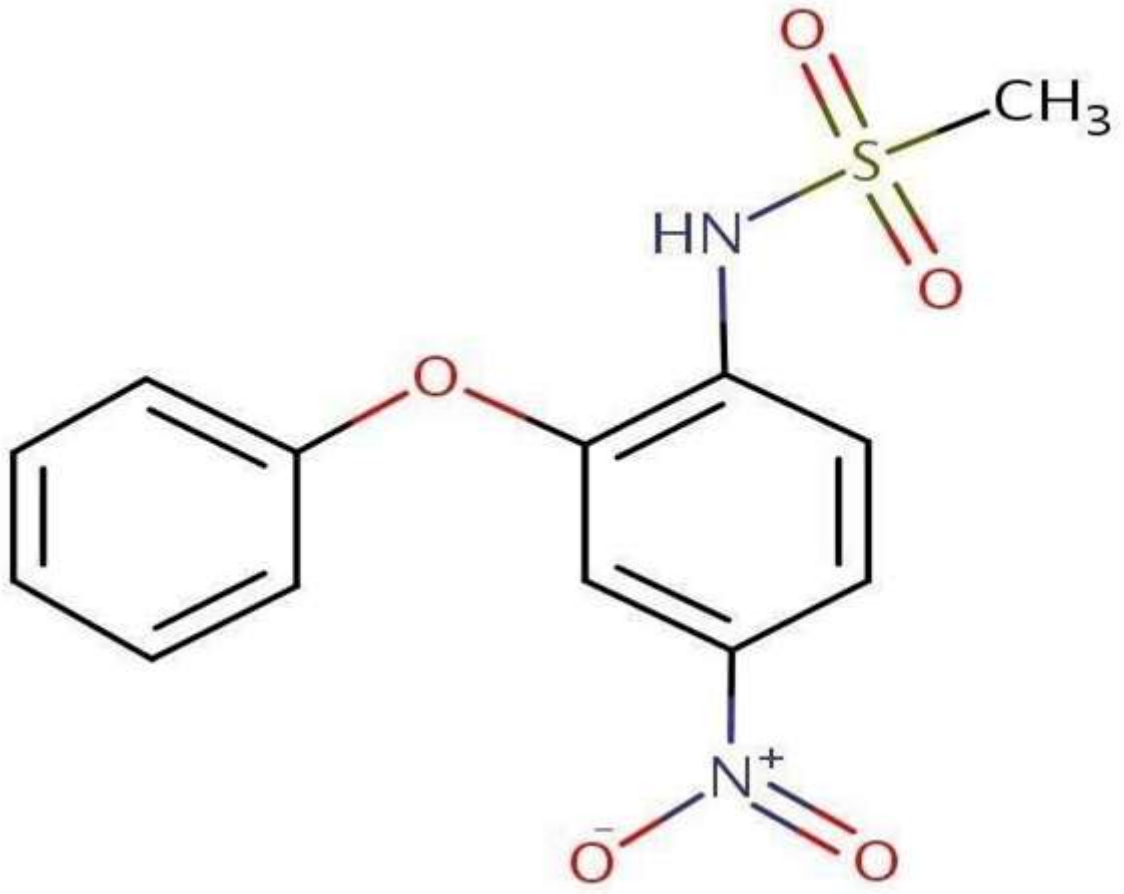
Summary:
'Nimesulideis a cyclooxygenase 2 inhibitor used to treat acute pain and primary dysmenorrhea.
Brand Names: Nimesulide
Generic Name: Nimesulide
DrugBank Accession Number: DB04743

Background :

Nimesulide is a relatively COX-2 selective, non-steroidal anti-inflammatory drug (NSAID) with analgesic and antipyretic properties. Its approved indications are the treatment of acute pain, the symptomatic treatment of osteoarthritis and primary dysmenorrhoea in adolescents and adults above 12 years old. Due to concerns about the risk of hepatotoxicity, nimesulide has been withdrawn from market in many countries.

Type: Small Molecule
Groups: Approved, Investigational
Weight: Average: 267.3639
Monoisotopic: 267.183443671
Chemical Formula : C13H12N2O5S
Synonyms: Nimesulide , Nimesulida

Structure:



Boiling Point: 442ºC (estimate)
Melting Point: 143 °C
Protein binding: >97.5%
Indication:
For the treatment of acute pain, the symptomatic treatment of osteoarthritis and primary dysmenorrhoea in adolescents and adults above 12 years old.

Mechanism of action:
The therapeutic effects of Nimesulide are the result of its complete mode of action which targets a number of key mediators of the inflammatory process such as: COX-2 mediated prostaglandins, free radicals, proteolytic enzymes and histamine.

Absorption:
Rapidly absorbed following oral administration.

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Metabolism: Hepatic. Extensive biotransformation, mainly to 4-hydroxynimesulide (which also appears to be biologically active).

Route of elimination: Renal (50%), fecal (29%)

Pharmacodynamics:
Nimesulide is a nonsteroidal anti-inflammatory drug(NSAID), acting specifically as a relatively selectivecyclooxygenase-2 inhibitor. However, the pharmacological profile of nimesulide is peculiar, and additional, unknown/yet-to-be-identified mechanisms appear to also be involved.One pathway that has been implicated in its actions is the ecto-5'-nucleotidase(adenosineA2A receptorpathway.

Pharmacokinetics:
Nimesulide is absorbed rapidly following oral administration.
Nimesulide undergoes extensive biotransformation, mainly to 4-hydroxynimesulide (which also appears to be biologically active).
Food, gender, and advanced age have negligible effects on nimesulide pharmacokinetics.
Moderate chronic kidney diseasedoes not necessitate dosage adjustment, while in patients with severe chronic kidney disease or liver disease, nimesulide is contraindicated.
Nimesulide has a relatively rapid onset of action, with meaningful reductions in pain and inflammation observed within 15 minutes from drug intake.
The therapeutic effects of nimesulide are the result of its complex mode of action, which targets a number of key mediators of the inflammatory process such as: COX-2 mediated prostaglandins, free radicals, proteolytic enzymes, and histamine. Clinical evidence is available to support a particularly good profile in terms of gastrointestinal tolerability.

Uses of NIMESULIDE:
Pain relief

Medicinal Benefits:
NIMESULIDE is composed of nimesulide, primarily used to treat mild to moderate pain due to its analgesic property. NIMESULIDE is prescribed mainly to treat pain and get relief from discomfort caused by conditions like tooth pain, arthritis, period pain, and other types of short-term pains. It helps in treating pain by blocking the chemical messenger in the brain responsible for causing fever, pain, and inflammation. Nimesulide works by blocking the effect of a chemical known as prostaglandin responsible for inducing pain and inflammation in our body.

Directions for Use:
Take it with food to avoid upsetting the stomach. Do not chew, crush, or break the tablet. Drink plenty of fluids while taking NIMESULIDE. Do not take it with dairy products like milk, yogurt, or calcium-fortified juices.

Storage:
Store in a cool and dry place away from sunlight

Side Effects of NIMESULIDE:
Most of the side effects of NIMESULIDE do not require medical attention and gradually resolve over time. However, if the side effects are persistent, reach out to your doctor. The most common side effects of NIMESULIDE are nausea, diarrhoea, changes in liver function tests, vomiting, and rash. Very rarely, it can cause an increased heart rate. It is not necessary for everyone to experience the above side effects. In case of any discomfort, speak with your doctor**.**

Adverse Effects:
The primary adverse effects of metoprolol include heart failure exacerbation, fatigue, depression, bradycardia or heart block, hypotension, bronchospasm, cold extremities, dizziness, decreased libido, diarrhea, tinnitus, decreased exercise tolerance, glucose intolerance, and may mask hypoglycemia. Abrupt cessation of the drug may lead to a withdrawal syndrome that could cause angina or myocardial infarction. Tachycardia and hypertension are both common in withdrawal syndrome.

Toxicity:
Treatment will vary based on the amount of metoprolol amount taken, comorbidities, age, and other co-investments. On arrival, assess ABCs and monitor appropriate blood work, including coingestants, ECG, large-bore IVs, and pregnancy status if female. Consult poison control/toxicology early in the course. Treatment choices include volume resuscitation, activated charcoal, whole bowel irrigation, nasogastric lavage, atropine, glucagon, calcium gluconate/calcium chloride, high-dose insulin, vasopressors, Intralipid, transcutaneous, or transvenous pacemaker. Cardiac status and a current fluid balance will guide volume

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resuscitation. Activated charcoal is typically given 1 g/kg and usually only has efficacy if dosed within 1 to 2 hours of ingestion.[15]If the patient has any altered mentation, caution is necessary to the possibility of aspiration. Whole bowel irrigation should be a consideration for extended-release preparations or large quantityingestion.

Formulation Aspects For Mouth Dissolving Films:

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. Dimenhydrinate can also be incorporated into ODFs for taste masking. Common examples of drugs incorporated into ODFs are salbutamol sulfate, rizatriptan benzoate, verapamil ondansetron, dexamethasone, rofecoxib, cetirizine,pilocarpine, tianeptine sodium, indomethacin, etc.

Film Forming Polymer:

Water-soluble polymers are used as film formers as they provide quick disintegration, good mouth feel, and mechanical strength to the films. The robustness of the strip depends on the type of polymer and its amount in the formulations. A variety of polymers are available for preparation of films of which pullulan, gelatin and hypromellose are most commonly used. Examples of watersoluble polymers include: Pullulan, Gelatin, guar gum, xanthan gum, Hydroxyl propyl methyl cellulose (HPMC), Modified starches, PVPK30, PVA etc. HPMCE3/E5/E6/E15.

Ideal properties of the polymers used in the oral film:

1. Polymers should be nontoxic, non- irritant andnon-bitter.
2. Polymers should betasteless
3. It should be devoid of leachableimpurities
4. It should be inexpensive and readilyavailable
5. It should not be an obstacle in the disintegrationtime
6. It should have good wetting and spreadibilityproperty
7. It should exhibit sufficient peel, shear and tensilestrength 8. It should not cause secondary infection in the oral cavity and should have sufficient shelflife.

Plastisizers:

In general, mechanical properties such as tensile strength and percent elongation are improved by adding plasticizer to the formulations. The concentration of plasticizer usually ranges from 0% to 20% w/w. Common examples of plasticizers are PEG, glycerol, diethyl phthalate, triethyl citrate, tributyl citrate, etc.

Sweetening Agent:

Sweeteners have become an important part of the food products as well as pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. Natural sweeteners as well as artificial sweeteners are used to improve the palatability of the mouth dissolving formulations. Some suitable sweetenersinclude:

(1) Water soluble natural sweetener: xylose, ribose, glucose, sucrose, maltose, steviosideetc.
(2) Water soluble artificial sweetener: sodium or calcium saccharin salts, acesulfame-Ketc.
(3) Dipeptide based sweetener:aspartame

Saliva Stimulating Agent:

Salivary stimulants are generally acidic in nature stimulating the production of saliva in buccal cavity, consequently, promoting the disintegrating of ODFs. Some commonly used saliva stimulating agents are citric acid, malic acid, tartaric acid, ascorbic acid and lacticacid.

Surfactant:

Surfactants are used as solubilizing or wetting or dispersing agents as a result that the film gets dissolved within seconds and release active agent immediately. Surfactants also improve the solubility of poorly soluble drugs in fast dissolving buccal films. E.g.: Polaxamer 407, sodium lauryl sulfate, benzalkonium chloride, benzthonium chloride, tweens and spans etc.

Flavor:

Flavors are needed to mask the bitter or nauseating taste of incorporated drug. Amount of flavor depends upon its nature and strength. Any US-FDA approved flavor can be used such as sweet, sour or mint flavor one of the research work verified that mint, licorice and sucralose mixture flavors appropriately mask the bitter taste of diclofenac sodium. Electronic tongues are used to discriminate the effect of various taste masking agents (TMAs)

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Colouring Agent:

Pigments such as titanium dioxide or FD&C approved coloring agents are incorporated (not exceeding concentration levels of 1%w/w) in oral strips when some of the formulation ingredients or drugs are present in insoluble or suspensionform.

Mechanism Of Film Formation:

Film forming system is applied directly to the skin and it forms a thin, transparent film in situ upon solvent evaporation as shown in fig. 1. After application of the formulation to the skin, the composition of the film forming system changes significantly due to the loss of the volatile components of the vehicle which results in formation of residual film on the skin surface. In this process the concentration of drug increases, reaching saturation level and with the possibility of reaching super saturation level on the skin surface. Supersaturation results in the enhanced drug flux through the skin by FFS creates supersaturated systems immediately after application to patch (EVRA®) through human epidermis in vitro. The film forming the skin, overcoming the problem of instability. Thus it improves the formulations showed a higher permeation than the commercial patch. drug permeation through skin compared to other transdermal dosage Without enhancer the formulation transported more than double the forms. The delivery efficiency of the film forming solutions for ethiny increasing the thermodynamic activity of the formulation without affecting the skin's barrier, thereby reducing the side effects or irritation.

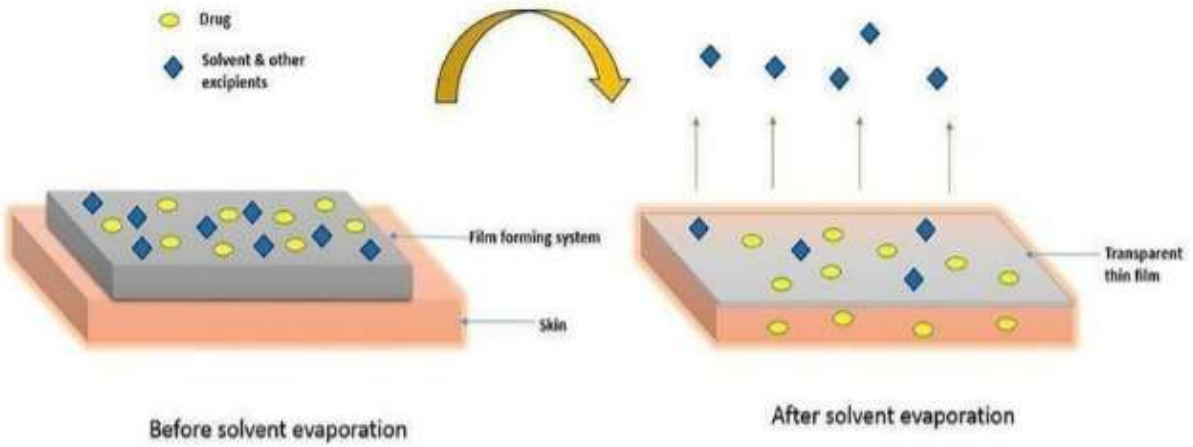

Fig. : Mechanism of film formation

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The concept of super saturation can be explained by the modified form of Fick's law of diffusion. Fick's law of diffusion given by Eq.

$$J = \frac{DKCv}{h}$$

Where

J = rate of drug permeation per unit area of skin per unit time (flux)
D = diffusion coefficient of drug
Cv= concentration of drug h =thickness of barrier to diffusion

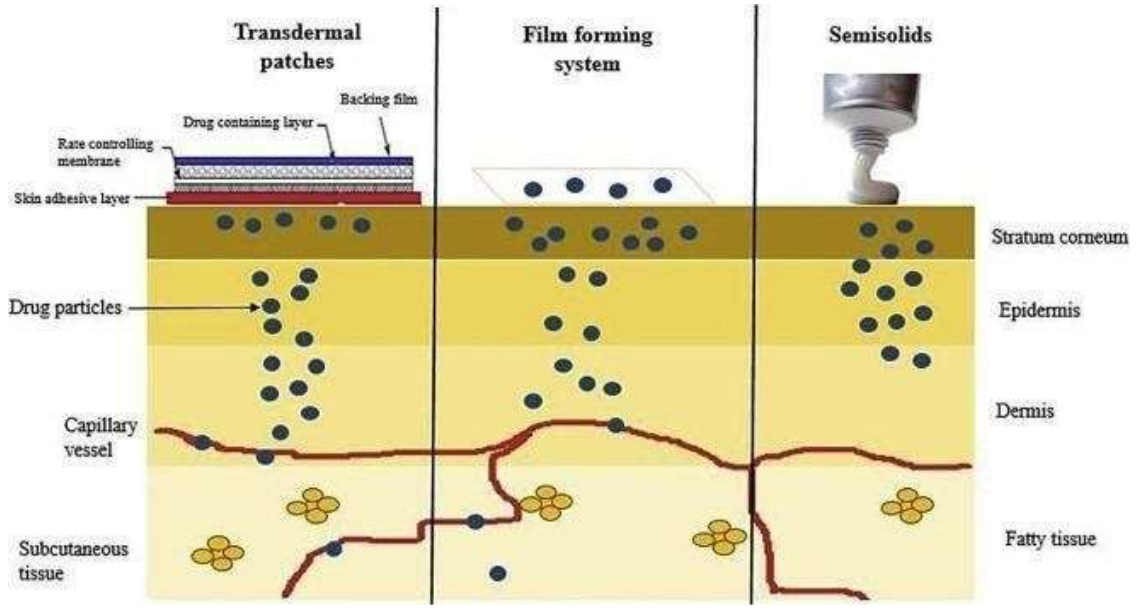

Fig. : Release Profile of the topical and transdermal drug delivery systems

Evaluation Of Film:

Weight variation of the film

One square inch film was cut at five different places in the caste film. The weight of each filmstrip was taken and the weight variation was calculated.

Thickness of the film

The thickness of the film was performed by screw gauge at different position of the film and the average thickness was calculated.

Tensile strength

Tensile strength of the film was determined with digital tensile tester, which consists of two load cell grips. The lower one is fixed and upper one is movable. The test film of specific size 3-inch X 10 mm was fixed between these two cell grips and force was gradually applied till the film breaks.

Percentage elongation

The Percentage elongation was carried out by using Hounsfield universal testing machine. It consists of two load cells grips. The lower one is fixed and upper one is movable. The test film of specific size 3-inch X 10 mm was fixed between these two cell grips and force was graduallyapplied till the film breaks. The readings were taken from the instrument. Folding endurance The folding endurance is expressed as the number of folds (number of times of film is folded at the same plain) required breaking the specimen or developing visible cracks. This gives an indication of brittleness of the film. A small strip of 4 square cm was subjected to this test by folding the film at the same plane repeatedly several times until a visible crack wasobserved.

Disintegration time

Test was performed using disintegration test apparatus. One square inch film was placed in the basket, raised and lowered it in such a manner

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that the complete up and down movement at a rate equivalent to thirty times a minute. Time required by the film, when no traces of film remain above the gauze was noted. Test was performed intriplicate.

Mouth dissolving time

The mouth dissolving time was determined by placing the film manually into a beaker containing 50 ml of 6.8- pH phosphate buffer. Time required by the film to dissolve was noted.

Content uniformity

The films were tested for content uniformity. Films of size one square inch was cut, placed in 100 ml volumetric flask and dissolved in methanol, volume was made upto 100 ml with methanol. Solution was suitably diluted. The absorbance of the solution was measured at 285 nm.

In-vitro dissolution studies

Dissolution profile of Mouth dissolving films were compared with pure drug. Dissolution study was carried out using USP type II (paddle apparatus) with 500 ml of 0.1 N HCl containing 0.5 % W/V Sodium Lauryl Sulphate, as dissolution medium maintained at 37 ±0.50 C. Medium was stirred at 100 rpm for a period of 1 hour. Samples were withdrawn at every 15-min interval, replacing the same amount with the fresh medium. Samples were suitable diluted with methanol and analyzed for drug content at 285 nm.

Method Of Preparation Of Mouth Dissolving Films:

Following processes can be used to manufacture fast dissolving films:

1. Solventcasting
2. Semi solidcasting
3. Hot melt extrusion
4. Solid dispersionextrusion
5. Rollingmethod

1. Solvent castingmethod

In solvent casting method water soluble polymers are dissolved in water and the drug along with other excipients is dissolved in suitable solvent then both the solutions are mixed and stirred and finally casted in to the Petri plate, dried and cut in to uniform dimensions. Londhe V Y and Umalkar K B were prepared fast dissolving film of Telmisartan by using solvent casting method.

2. Semi solid castingmethod

In semisolid casting method firstly a solution of water-soluble film forming polymer is prepared. The resulting solution is added to a solution of acid insoluble polymer (e.g. cellulose acetate phthalate, cellulose acetate butyrate), which was prepared in ammonium or sodium hydroxide. Then appropriate amount of plasticizer is added so that a gel mass is obtained. Finally the gel mass is casted in to the films or ribbons using heat controlled drums. The thickness of the film is about 0.015-0.05 inches. The ratio of the acid insoluble polymer to film forming polymer should be1:4.

3. Hot melt extrusion method

In hot melt extrusion method firstly the drug is mixed with carriers in solid form. Then the extruder having heaters melts the mixture. Finally the melt is shaped in to films by the dies. There are certain benefits of hot melt extrusion.

· Fewer operationunits
· Better contentuniformity
· An anhydrousprocess.

Cilurzo F et al. developed fast dissolving film containing maltodextrin using hotmelt extrusion technology.

4. Solid dispersion extrusion

In this method immiscible components are extrude with drug and then solid dispersions are prepared. Finally the solid dispersions are shaped in to films by means of dies.

5. Rolling method

In rolling method a solution or suspension containing drug is rolled on a carrier. The solvent is mainly water and mixture of water and alcohol. The film is dried on the rollers and cut in to desired shapes and sizes.

Preparation Of Mouth Dissolving Films By Using Nimesulide:

Procedure :

1) Solvent casting method involves firstly the water soluble polymers are dissolved in water at 1,000 rpm and can be heated up to60°C.
2) All the other excipients like colors, flavoring agent, sweetening agent, etc., are dissolved separately.
3) Then both the solutions obtained are mixed thoroughly stirring at 1,000rpm.
4) The obtained solution is incorporated with the API dissolved in suitablesolvent.
5) The entrapped air is removed byvacuum.

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6) The resulting solution is cast as a film and allowed todry.
7) which is then cut into pieces of the desired size.
And then single punch tablet press and multi station/rotary tabletpress.
8) And lastpackaging.

Formulation of Nimesulide MDT:

Sr.no	Ingredients	Formulation					Role of Ingredient
	Formulation code	F1	F2	F3	F4	F5	
1)	Nimesulide	13.03	13.03	13.03	13.03	13.03	Drug
2)	Xanthan gum(mg)	65.18	97.78	130.3	162.9	195.5	Suspending agent
3)	Poly ethylene glycol 400(ml)	0.26	0.26	0.26	0.26	0.26	Surfactant
4)	Sodiumstarch glycolate(mg)	6.51	6.51	6.51	6.51	6.51	Super disintegrate
5)	Citric acid (mg)	3.25	3.25	3.25	3.25	3.25	Preservative
6)	Sucrose(mg)	3.25	3.25	3.25	3.25	3.25	Filler
7)	Vanillin(mg)	3.25	3.25	3.25	3.25	3.25	Flavoring agent
8)	Amaranth(mg)	q.s	q.s	q.s	q.s	q.s	Colouring agent
9)	Water(ml)	5.21	5.21	5.21	5.21	5.21	Vehicle

Defects of mouth

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III. RESULTS AND DISCUSSION:

The use of superdisintegrants for preparation of mouth dissolving tablets is highly effective and commercially feasible. The results of tablets were evaluated for uniformity of weight, thickness, hardness, friability, wetting time, water absorption ratio, disintegration time and dissolution study (Table 2). Using the same excipients, the tablets were prepared, without these superdisintegrants accelerate disintegration of tablets by virtue of their ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking of tablets and therefore faster disintegration. This disintegration is reported to have an effect on dissolution characteristics as well. Prepared mouth-dissolving tablet gets dispersed in the mouth quickly and releases the drug early as compared to its formulated conventional tablet. Figure 1 show the cumulative percentage of Nimesulide released from formulated tablet with different concentration of Crosscarmellose sodium and Sodium starch glycolate. It is clear that the dissolution of Nimesulide has improved considerably in formulation P4 as compared to formulation P1, P2, P3 and P5 (Control). The tablets of the batch P4 showed good dissolution efficiency and rapid dissolution.

IV. CONCLUSIONS:

In the present study the superdisintegrant property of locust bean gum has been explored. Extensive swelling, porosity and wicking action of the natural material in the orodispersible tablet formulation were found to be contributing its superdisintegrant action. The tablets disintegrated much faster and consistently when locust bean gum was used as superdisintegrant compared to cross carmellose sodium. Locust bean gum and modified locust bean gum could be used for different applications in tablet dosage forms and may be explored as high functionality excipient for future applications.

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