International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1236-1247 www.ijprajournal.com ISSN: 2249-7781

"Comparative Study of Orodispersable Granules Amd Mouth Dissolving Films"

Sehrash Ansari[1*], Sheela Yadav[2], Mohammed Jahid Halder[1], Zahid Ansari[1], Kadir Ansari[1], Badal Yadav[1],

H.k. college of pharmacy, jogeshwari (west), mumbai – 400102.

Date of Submission: 01-08-2021 Date of Acceptance: 18-08-2021

ABSTRACT : Mouth Dissolving Drug Delivery System (MDDDs) has of late become a crucial route of drug administration. The utilization of sticky bag of Orodispersable granules referred to as quick dissolving granules is most typical. Mouth strip could be a sort of strips that is employed in acute condition like pain, antiemetic, and Emmet headache. During this we've studied the comparative study of the mouth dissolving films and mouth dissolving granules. The literary criticism consists of methodology, benefits and drawbacks, challenges visaged throughout the formulation. The strategy used for formulating films square measure solid Casting methodology, Hot soften Extrusions, Rolling methodology and for granules we tend to used Wet Granulation and Dry Granulation. The dosages forms square measure placed within the mouth, allowed to disperse or dissolve within the spit, then square measure enveloped within the traditional means. Weight variation, Folding Endurance, Disintegration and Dissolution is dole out for Films. Bulk Density, Hausner quantitative relation, tapped density square measure dole out for Granules. Challenges like quality of Drug, style Masking Stability and Dose Uniformity etc. for Films. The Comparisons and analysis of films and granules square measure all over within the article.

I. INTRODUCTION

MOUTH DISSOLVING DRUG DELIVERY SYSTEMS:

Mouth Dissolving Drug Delivery System (MDDDs) has become progressively necessary attributable to their distinctive properties. They quickly disintegrate and dissolve, and may be administered while not water, creating them notably appropriate for medicine and geriatric patients.

Mouth Dissolving Drug Delivery System (MDDDs) has late become a vital route of drug administration. varied bio adhesive tissue layer dose forms are developed, which incorporates adhesive granules, gels, ointments, granules, patches and a lot of recently the employment of chemical compound strips for mouth delivery, additionally called mouth dissolving strips. The employment of sticky bag of orodisperable granules called quick dissolving granules.

Oral route of drug administration has wide acceptance up to 50–60% of total folk's expertise inconvenience in swallowing standard dose forms like granules once water isn't obtainable, within the case of kinetosis (kinetosis) and abrupt episodes of coughing throughout the cold, allergic conditions, and respiratory illness. For these reasons, granules that may chop-chop dissolve or disintegrate within the rimaoris have attracted an excellent deal of attention.

The solubility of sure medicine presents a challenge to the formulator for developing an acceptable oral formulation. The bioavailability of poorly soluble drug is commonly restricted by its dissolution rate that successively is controlled by the expanse obtainable for dissolution. For such medicine, solid dispersion could be an important approach to attain reduction in size and increase in solubility and thus, dissolution characteristics.

Formulating mouth dissolving granules victimization solid dispersion of drug shall not solely improve solubility and subsequent bioavailability however additionally improved patient compliance and convenience.

The combination of solid dispersion and mouth dissolving films or granules technology area unit needed to deal with the matter of low bioavailability.

Many patients have problem swallowing granules and laborious gelatin capsules and consequently don't take medications as prescribed. It's calculable that fifty of the population is littered with this downside, which ends up in an exceedingly high incidence of rebelliousness and ineffective medical aid.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1236-1247 www.ijprajournal.com ISSN: 2249-7781

The problem may be resolved by the creation of quick drug delivery system (FDDS), which do not need water to help swallowing. The dosages forms area unit placed within the mouth, allowed to disperse or dissolve within the spittle, so area unit enclosed within the traditional method.

MOUTH DISSOLVING STRIPS:

Mouth dissolving strips could be a new drug delivery system for oral delivery of drug. Mouth strip could be a style of strips that is employed in acute condition like pain, antiemetic, pismire megrim, anti-hypertension, symptom heart condition, and respiratory illness etc.

Mouth dissolving strips has gained quality thanks to its availableness in varied size and form. Mouth dissolving strips area unit supposed that disintegrate or dissolve among seconds. they provide many blessings like administration while not water, fast onset of action and convenience of dosing. For quick dissolving active pharmaceutical ingredients absorption is feasible through the oral mucous membrane and will improve bioavailability of the medicine.

These Orodispersable films area unit specialised in an exceedingly method that the water isn't needed for administration as a result of they quickly fragment among a couple of seconds, discharging the drug in mouth.

Orodispersable films, at the purpose once assault tongue, right away hydrates by soaking spittle following disintegration and/or dissolution discharging active pharmaceutical agent from the dose type.

No high-cost lyophilization, high mechanical strength, fast disintegration, and small choking risks area unit the standard attributes/or hallmarks of ODFs.

The explanation of possessing distinctive properties and fast disintegration time starting from seconds to a minimum of one minute have attained exceptional significance in pharmaceutical trade business and patient compliance.

ODFs vogue permits to incorporate a variety of medicines for his or her pharmacologic effects e.g., expectorator, anti-tussive, antiasthmatic, anti-epileptic etc.

ODFs area unit quick disintegrating skinny films having a vicinity starting from five to twenty cm2 within which active pharmaceutical ingredient (API) is consolidated within the style of matrix utilizing hydrophilic compound. Active pharmaceutical ingredient area unit typically consolidated up to fifteen mg in conjunction with different excipients i.e., plasticizers, sweeteners, style modifiers, colorant

ORODISPERSABLE GRANULES:

Orodispersable granules also are known as as orally disintegrating granules, mouth-dissolving granules, fast dissolving granules, fast-disintegrating granules, and fast-dissolving granules.

Despite of tremendous advancements in drug delivery, the oral route remains the proper route for the administration of therapeutic agents attributable to low value of medical aid, simple administration, correct dose, self-medication, pain dodging, skillfulness, resulting in high levels of patient compliance.

Orally Disintegrating Granules (ODG) disintegrate and/or dissolve chop-chop within the spittle while not the requirement for water. Some granules area unit designed to dissolve in spittle remarkably quick, among a couple of seconds, and area unit true fastdissolving granules.

ODG area unit administered while not water. Granules manufacture particle-size uniformity, so content uniformity. Granules increase compressibility.

ANATOMY OF ORAL CAVITY:

The structure and anatomy of mouth is studied for understanding the surroundings provided for delivering medication. The oral mucous membrane permits direct access of drug to the circulation and avoids initial pass metabolism.

The epithelial tissue of the mouth is sort of the same as that of the skin, with slight variations with relevancy organic process, protecting and stuff mucosa that is unfold across its surface.

The porousness of oral mucous membrane is 4–1000 times larger than that of the skin. The mouth is split into 2 regions: outer being the oral vestibule delimited by the lips and cheeks; the exhausting and soft palates, the ground of the mouth and tonsils.

Oral drug delivery has been far-famed for many years because the most generally used route of administration among all the routes that are explored for the general delivery of medicine via numerous pharmaceutical merchandise of various indefinite quantity forms.

THE IDEAL CHARACTERISTICS OF DRUG TO BE SELECTED:

- The drug ought to have pleasant style.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1236-1247 www.ijprajournal.com ISSN: 2249-7781

- The drug ought to have little molecular size and low mass.
- The drug ought to have sensible solubility and stability in water in addition as in spit.
- It ought to be partly unionized at the hydrogen ion concentration of mouth.
- The drug ought to exhibit low sensitivity to environmental conditions.
- It ought to have the flexibility to permeate oral tissue layer tissue. The therapeutic dose of the drug mustn't be larger than 40mg.

COMPARATIVE STUDY OF ORAL FAST DISINTEGRATING FILMS AND ORAL DISPERSABLE GRANULES:

Sr.no	Mouth Dissolving Films	Orodispersable Granules
1.	It is in the form of Films	It is in the form of granules
2.	Dissolution rate is greater due to large surface area	Dissolution rate is lesser due to small surface area
3.	It is more patient compliance	It is less patient compliance
4.	In this low dose can be incorporated	In this high dose can be incorporated
5.	Films are more flexible and durable	Granules are less durable
6.	Faster onset of action	Slower onset of action
7.	It reduces the 1^{St} Pass Metabolism	There is no such advantage
8.	There is no risk of Choking	There is fear of Choking
9.	It can be given to geriatric and paediatric patient	It cannot be given to geriatric and paediatric patient
10.	It is used in unconscious people	It cannot be given to unconscious people
11.	Disintegration is faster	Disintegration requires time
12.	Better taste masking and enhanced stability	Cannot completely mask the taste
13.	Water is not required for administration	Water is not required for administration
14.	It is available in very thin films	It is in small granulated sizes
15.	It does not require granulation	Granulation is required

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1236-1247 www.ijprajournal.com ISSN: 2249-7781

16.	pH should be 7	pH should be similar to surface area of mouth

METHOD OF PREPARATION OF MOUTH DISSOLVING FILMS:

One or combination of the subsequent ways will be used for the preparation of mouth dissolving strips.

- Solvent casting
- Semisolid casting
- Hot soften extrusion
- Rolling methodology.

Solvent Casting Method:

- It is ready by solvent casting methodology exploitation HPMC as a movie base with completely different concentration. PEG-400 used as plasticiser
- Mannitol, sweetener used as sweetener
- Citric acid used as secretion stimulating agent
- CCS and SSG used as disintegrating agent
- Polymers are dissolved in water by exploitation magnetic stirrer
- Mannitol, aspartame, acid, CCs, SSG and PEG-400 were side to the compound answer and stirred for two minutes on a magnetic stirrer
- Active pharmaceutical ingredient was side at the side of paracetamol to on top of answer underneath continuous stirring for two minutes.
- Sonicated for five min to get rid of bubble
- Solution casted on Petri dish and dried in hot air kitchen appliance at four hundred C for twelve hours
- Films were fastidiously aloof from Petri dish. look into the imperfections and cut in needed size Stored in desiccator for additional analysis **Semisolid Casting method:**
- Solution of the soluble strips forming compound is ready
- Resulting answer is then side to the answer of acid insoluble compound
- Appropriate quantity of plasticiser is side to obtained a gel mass
- Gel mass is then casted onto the strips or on ribbons exploitation heat-controlled drums
- The thickness of the film ought to be concerning zero.015-0.05 inches. The magnitude relation of the acid insoluble compound to the film forming compound ought to be 1:4 **Hot soften Extrusion method:**
- The drug is mixed with carriers within the solid kind Extruder having heater melts the mixture.
- Finally, the molten mixture is formed in a very film by the dies **Rolling method:**
- In rolling methodology, an answer or suspension of drug with strips forming compound is ready and subjected to the roller.
- The answer or suspension ought to have specific physical science thought.
- The solvent is principally water and mixture of water and alcohol.
- The strip is dried on the rollers and cut in to desired shapes and sizes.

METHOD OF PREPARATION OF ORODISPERSABLE GRANULES:

- Granules are agglomerates of fine materials ready into larger, free flowing particles.
- They usually fall among the vary of 850 µm (No. twenty sieve) to four.75mm (No. four sieve) size. The shape of granules is usually irregular.
- Granules are sometimes created as a step to organize granules.
- Granule's flow into the dies a lot of equally and a lot of freely than particles from the hopper (the funnel-like instrumentality holding the drug to guide its flow into the tableting press).
- Granules are sometimes created as a step to organize granules. Granule's flow into the dies a lot of equally and a lot of freely than particles from the hopper (the funnel-like instrumentality holding the drug to guide its flow into the tableting press).

Advantages of granules are listed below:

- Granules shows sensible flow properties. The straightforward flow characteristics are vital in activity drug materials from the hopper or feeding instrumentality into the tableting presses. For this reason, powder mixtures are sometimes coarse if they're supposed to be compressed into granules. Granules conjointly eliminate or management dirt. Granules increase sponginess.
- Granules have smaller extent than a comparable volume of powders. This makes granules a lot of stable physically and with chemicals than the corresponding powders. Granules are less possible to cake or harden upon standing than are powders.
- Granules are a lot of simply wetted by a solvent than are bound powders, in order that

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1236-1247 www.ijprajournal.com ISSN: 2249-7781

granules are most well-liked in creating solutions.

- Granules turn out particle-size uniformity, therefore content uniformity. Granules forestall segregation of constituents of powder mixture.

Wet Granulation:

Wet granulation or dampish granulation is that the most standard, versatile and wide used techniques for the manufacture of compressed granules, because it imparts all the physical properties to the granules. This method differs from the opposite granulation ways because it involves the usage of liquids to create compact lots.

Wet Granulation procedure:

- Grinding Drug is side to the granulator and grinde.
- Blending or admixture the appropriate adjuvants (Ex. thinner and different excipients) are side and mixed in a very liquidiser.
- Shear admixture Granulating liquids (Ex. Alcohols) are side to create a moist mass of the fine material that resembles agglomerates.
- Wet screening the mass is screened to create pellets or granules.
- Drying the pellets or granules are dried to get rid of far more than the liquid.
- Dry screening Dry screening of granules leads to size reduction.

Dry Granulation:

The process of dry granulation is additionally referred to as Double Compression or Compression Granulation or Pre-Compression Granulation. The process involves the formation of pill by 1st changing the pill formulation into slugs or compact lots. These shaped lots are screened to create uniform sized fine granules. The technique is appropriate for those medicine that are wetness sensitive, degrade at higher temperature and administered in higher doses.

The technique of Dry granulation of fine material will be accomplished by 2 ways.

(a)Slugging (slug formation). (b)Roller compaction methodology.

Dry Granulation procedure:

- Grinding Drug is side to the granulator and grinded.
- Blending or admixture the appropriate adjuvants (Ex. thinner and different excipients) are side and mixed in a very liquidiser.
- Compaction when admixture, the powder mixture is slugged or compressed into massive flat granules or pellets concerning one in. diameter. On massive scale, Roller compactor is most well-liked.
- Crushing these slugs are weakened by hand or by edge to create granules
- Screening or winnow the granules bear dry screening through a desired mesh for size.

EVALAUATION PARAMETERS OF MOUTH DISSOLVING FILMS:

General analysis of Mouth Dissolving Films:

Weight Variation: - For analysis of strips weight, 3 strips of each formulation area unit designated every which way and individual weight of every 2x2 cm strip was taken on digital balance. The typical weight was calculated.

Thickness: - Because the thickness of strip is directly concern with drug content uniformity thus it's necessary to establish uniformity within the thickness of the strip. It are often measured by micrometre screw gauge or label digital Vernier Callipers at totally different strategic locations.

Dryness Test/Tack Test: - Concerning eight stages of strip drying method are known and that they area unit set to the touch, dust free, tack free (surface dry), Dry to the touch, dry hard, dry through (dry to handle), dry to recoat and dry print free. Though these tests area unit primarily used for paint films most of the studies are often custom-made in an elaborate way to gauge pharmaceutical Mouth Dissolving Strips. The main points of analysis of those parameters are often checked elsewhere and area unit on the far side the scope of this review. Tack is that the determination with that the strip adheres to an adjunct (a piece of paper) that has been ironed into contact with the strip. Instruments are out there for this study.

Surface pH of Strip: - Surface pH of the strip made up our minds by inserting the strip and permit to swell in closed dish at temperature for thirty min. in ten mil phosphate buffers (pH half dozen.8). The answer was placed below digital pH meter electrodes. The modification within the pH was determined and reported.

Tensile Strength: - Lastingness is that the most stress applied to some extent at that the strips specimen breaks. It's calculated by the applied load at rupture divided by the cross-sectional space of the strip as given within the equation below:

Tensile strength = Load at breakage Strip thickness × Strip dimension

Percentage Elongation: - once stress is applied, a strip sample stretches and this can be spoken as strain. Strain is largely the deformation of strip

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1236-1247 www.ijprajournal.com ISSN: 2249-7781

divided by original dimension of the sample. Generally, elongation of strip will increase because the plasticiser content will increase.

% Elongation = Increase long ×100 Original length

Folding Endurance: - Folding endurance is set by perennial folding of the strip at a similar place until the strip breaks. The quantity of times the strip is rolled while not breaking is computed because the folding endurance price.

Disintegration Time: - Disintegration of Mouth Dissolving strips need USP disintegration equipment. The disintegration point in time of thirty seconds or less for orally disintegrating granules represented in CDER steering are often applied to quick dissolving oral strips. Disintegration time can vary reckoning on the formulation however usually the disintegration ranges from five to thirty seconds. Although, no official steering is offered for Mouth Dissolving strips.

Assay /Content Uniformity: -this can be determined by any customary assay methodology represented for the actual API in any of the quality assemblage. Content uniformity is set by estimating the API content in individual strip. Limit of content uniformity is 85–115 p.c (%).

Organoleptic analysis for analysis of psychophysical analysis of the merchandise, special controlled human style panels area unit used. In-vitro strategies of utilizing style sensors, particularly designed equipment and drug unharness by changed assemblage strategies area unit being employed for this purpose. These invitro style assessment equipment and methodologies area unit similar temperament for prime output style screening of oral pharmaceutical formulations.

Swelling Property: - Strips swelling studies is conducted victimization simulated secretion answer. Every strip sample is weighed and placed in an exceedingly reweighed stainless-steel wire mesh. The mesh containing strip sample is submerged into 15ml medium in an exceedingly plastic instrumentation. Increase within the weight of the strip made up our minds at the present interval till a relentless weight was determined. The degree of swelling was calculated victimization parameters α = wt - wo/wo wt is weight of strip at time t, and wo is weight of strip at time zero

Transparency: - The transparency of the strip are often determined employing a straightforward ultraviolet photometer. Cut the strip samples into rectangles and placed on the interior facet of the photometer cell. The verify coefficient of strips at 600 nm. The transparency of the strips was calculated as follows.

Transparency = (logT600)/b = - €c

Where T600 is that the coefficient at 600 nm and b is strips thickness (mm) & c is concentration.

In-Vitro Dissolution Study: - Dissolution testing are often performed victimization the quality basket or paddle equipment represented in any of the assemblage. The dissolution medium can basically be designated as per the sink conditions and highest dose of the API. Many times, the dissolution take a look at are often tough because of tendency of the strip to float onto the dissolution medium once the paddle equipment is utilized.

Stability Study: - A Stability study of the ready strip was distributed by storing strips in associate aluminum package for thirty days at four C/ seventy fifth RH, thirty C/75% RH and forty C/ seventy fifth RH. The strips were determined for activity (form and colour), disintegration time and drug content. Mouth dissolving strips were found to be physically and with chemicals stable as they showed no important modification in terms of physical characteristics (no discoloration & no modification in shape), disintegration time and drug content below all the storage conditions.

GENERAL ANALYSIS OF ORODISPERSABLE GRANULES:

Bulk Density: -Bulk density of powder make up my mind by running 2gm of sample mix gently through a glass funnel into a 10ml of graduate. The amount that is occupied by the sample was recorded, and bulk density is finally calculated by victimisation following formula.

Bulk density = weight of powder/ volume of powder in mensuration cylinder.

Tap Density: - at the start 2gm of sample mix was introduced during a 10ml of mensuration cylinder, so the initial volume of mix in cylinder is recorded. Finally faucet the cylinder incessantly till no any amendment in volume was noted. Finally faucet density was calculated by victimisation following formula.

Tap Density = weight of powder / faucetped volume of powder in mensuration cylinder.

Angle of Repose: - The angle of repose make up my mind by victimisation fix funnel methodology. The accurately weighted powder was allowed to flow through the funnel. The funnel is adjusted to a stand at definite height. The radius of powder and height of heap of cone was measured.

The angle of repose was then calculated by following formula.

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1236-1247 www.ijprajournal.com ISSN: 2249-7781

Tan θ = h / r
θ = tan-1(h/r)
Where, θ = angle of repose h = height of the heap r = radius of the heap

Compressibility Index: - The flow ability of powder may be determined by examination the majority density and broached density of powder. Carr's index was calculated by victimisation following
Carr's index = (tap density – bulk density) ×100 / faucet density

Hausner quantitative relation: -Hausner ratio is said to inhume particle friction and in and of itself accustomed predict powder flow property. Hauser quantitative relation of every pill mix was calculated by victimisation following
Formula= broached density / bulk density
Granule Strength and Friability: they're vital as a result of they affect:
Changes in particle size distribution of granulations. softness into cohesive granules. Grain strength and crumbliness area unit measured by:
Compressive strength / hardness
Using crumbliness measurements / equipment

Moisture content: - The quantity of wet gift within the grain is named wet content. Generally, granules contain a pair of wet. It's needed for the binding of the powder or granules throughout compression in die cavity. Proportion of wet is calculated by victimisation wet balance or IR balance. IR balance incorporates easy balance that is placed to the casing {in that during which within which} the IR bulb is connected which turn out heat within the chamber. The little quantity of sample taken from kitchen appliance to live wet content and place within the wet balance. Initial reading ought to be publish then we have a tendency to area unit initiating the IR bulb. As IR bulb is initiated the wet is off from the granules via heating then publish the reading % moisture content = initial weight – final weight / initial weight x 100

Sr.no	Evaluation of Films	Evaluation of Granules
1.	Weight of strips is weighed by taking the average of the strips	The weight is carried out after the formulation of the granules
2.	The thickness of the strip is measured by vernier calliper	The density of granules is determined using the Bulk density, Tap Density.
3.	The folding endurance of the films are evaluated	The flow of the granules is measured using angle of repose method.
4.	Dryness Test or Tack test is performed for Films	Moisture content test is performed for Granules.
5.	The tensile strength of films is evaluated by applying stress to it	The granules strength and friability are evaluated using different apparatus for friability and compression.
6.	Surface pH is determined using the buffers.	pH is evaluated for the granules.
7.	The Dissolution and Disintegration is done using the apparatus	The Dissolution and Disintegration is performed while maintaining same environment as that of oral route.
8.	Transparency test is carried out using UV Spectrophotometer.	There is NO Transparency test for granules.
9.	Swelling property of films is carried out using saliva simulated	The swelling property is not performed for granules

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1236-1247 www.ijprajournal.com ISSN: 2249-7781

	solution.	
10.	Stability is carried out keeping the film at room temperature	Stability is done to check the agglomeration and sogginess of the granules.
11.	Content Uniformity is carried out for even distribution of the Drug	The assay is carried for the content uniformity of the API
12.	Organoleptic Evaluation is done to maintain the physical Appearance.	Organoleptic Evaluation is done to maintain the physical Appearance.

CHALLENGES FACED FOR FORMULATING OF FILMS:

1) Insolubility of drug
2) Taste masking of bitter and objectionable drug
3) Reduction in drying time of film 4) High dose incorporation in film
5) Co-administration of medication
6) Stability of film against wetness and temperature
7) Need special packaging
8) Dose uniformity

Insolubility of drug:-

Solubility plays a rate limiting parameter to urge desired concentration of drug of orally administered formulation in circulation drawback of solubility may be a main challenge for formulation of oral film of BCS category II medication having low solubility and high porousness.

It is the foremost vital preference of a drug candidate to be elite for formulation of oral film.

In case of oral film, solubility plays a crucial role in 2 stages i.e., solubility of drug in solvent throughout formulation and solubility or dissolution of drug in secretion when golf shot the film in rima.

So, the solubility behaviour of drug remains one amongst the foremost difficult aspects in formulation of oral film.

Techniques for solubility improvement in oral film:

Hydrotrophy:-

Hydrotropic result suggests that the rise in saturation solubility of a substance in water by the addition of either organic salts or nonelectrolytes that should be physiologically compatible for pharmaceutical application.

These hydrotropic substances are able to increase the amount of element bridges within the water clusters.

This makes the water additional hydrophobic and therefore it's a much better solvent for non-polar drug.

Co-solvency: -

It is the most effective and simple technique in oral film formulation.

It is outlined because the addition of a water – miscible or partly compatible organic solvent (i.e., co-solvent to water) to extend solubility of a non-ionic drug.

Co-solvents are mixtures of water and one or additional water compatible solvents accustomed produce an answer with increased solubility for poorly soluble compounds

Taste masking of bitter and obnoxious drug:-

Taste is an important parameter just in case of quick dissolving oral film. Oral film must stay in-tuned with oral membrane till it Completely dissolves in secretion in rima.

For this, style of bitter medication ought to be cloaked. So, style masking becomes a necessity for bitter medication utilized in quick dissolving oral film to boost the patient compliance particularly within the medical specialty and geriatric population **Taste masking techniques:-**

Taste masking with sweeteners and flavours

This is terribly straightforward and principally used technique for oral film formulation. Terribly minimum quantity of sweetener and flavour are needed for formulation to mask the bitter style of drug.

Generally, sweeteners are utilized in the concentration of three to six w/w either alone or together.

Sweeteners play a crucial role in food merchandise & pharmaceutical dose forms that are disintegrated or dissolved in rima. The sweetness of style in

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1236-1247 www.ijprajournal.com ISSN: 2249-7781

formulation is additional most popular by medical specialty population.

Reduction in Drying Time: -
Drying time plays a crucial role in oral film formulation and additionally just in case of rate of production of oral film in industries.
Generally, hot air kitchen appliance isn't used for drying of oral film of thermo labile medication. So, oral film is dried at temperature. However it takes longer to dry (about one day).
Time taken by formulation for drying was found to be twenty four hours at 50°C for the formulation of quick dissolving oral film of Salbutamol sulfate investigated by Prasanthi N. L.et.al. (2011)

Reduction in drying time is achieved by following ways: - 1. By increase in temperature while not developing cracks to film.
2. choice of ingredients in film specially sort and concentration of compound and softener i.e., addition of these polymers and plasticizers that type less viscous resolution so drying time are minimum and bar of use of these polymers and plasticizers that type extremely viscous resolution so drying time are exaggerated.
3. Drying time is reduced by use of appropriate dryers.
4. Increase in space of film can expose giant surface to drying atmosphere and additional can scale back drying time.

High dose incorporation in film:-
Dose of drug in oral film formulation is exaggerated by increasing space of instrumentation.
Only space ought to be exaggerated keeping thickness of formulation resolution constant so volume of resolution required for formulation {is additionally|is additionally} exaggerated that facilitate in incorporation of high dose and reduction in drying time also.
If dish is taken into account as an instrumentation, then volume of formulation resolution is given below.
Volume of formulation resolution = space of dish × depth of formulation resolution in dish = x 0.35 cm
Volume of formulation resolution = 0.35 cm3 **Co-administration of medication:-**
Use of over one drug i.e., co- administration of medication may be a terribly troublesome task in oral film formulation.
Because, it's going to have an effect on disintegration time furthermore as dissolution rate of formulation.

Stability of film against wetness and temperature:-
Fast dissolving oral film consists of regarding forty fifth of compound that is deliquescent in nature.
In the wet atmosphere, film can absorb water and obtain liquefied thanks to dissolution of film in water. So, the steadiness of film against wetness is extremely troublesome and difficult task.
Though oral film formulation is that the best technique to forestall drug chemical phenomenon, it shows chemical phenomenon of drug at higher wetness and temperature conditions. **Need special packaging:-**
In the pharmaceutical business, it's important that the package elite adequately preserve the integrity of the merchandise.
A variety of packaging choices are obtainable for quick dissolving films. Associate in nursing atomic number 13 pouch is that the most ordinarily used packaging material.
APR Labtec developed the speedy card, proprietary packaging system designed for the speedy films. The speedy card has same size as a mastercard and holds 3 speedy films on all sides. Each dose is taken out severally.

Dose uniformity:-
Film that is to be created during an instrumentation should dig desired space containing needed dose of drug. So, to induce a consistent dose all told films that dig desired space could be a difficult task.
Content uniformity is measured by assay methodology of drug determined by specification in several collection.
It is determined by estimating the API content in individual film.
Limit of content uniformity ought to be 85- one hundred and fifteenth

CHALLENGES FACED FOR FORMULATING GRANULES:
1.Hygroscopic and Deliquescent Problem
2.Efflorescent powders Problem
3. Eutectic Mixtures.
4. Potent Drug Problem
5. Incompatible salts

Hygroscopic and Deliquescent Problem:

International Journal of Pharmaceutical Research and Applications
Volume 6, Issue 4 July-Aug 2021, pp: 1236-1247 www.ijprajournal.com ISSN: 2249-7781

Problem: - Absorption of wet from air resulting in partial or complete phase transition.
Solution: - A- Applied during a granular kind to decrease the exposed surface to air. B- Packed in tin foil or in wrap packets.

Efflorescent Powders Problem:
Problem: -Crystalline substances that throughout storage lose their water of crystallization and alter to powder (to be efflorescent). The liberated water converts the powder to a paste or to a liquid.
Solution: - Victimization the anhydrous kind, and treating it during a manner just like absorptive powders.

Eutectic Mixtures:
Problem: - Mixture of gear that liquefy once mixed, rubbed or triturated along. The melting points of the many mixture mixtures are below temperature.
Solution: - Victimization inert adsorbent like starch, talc, milk sugar to forestall wetness of the powder.

Potent Drug:
Problem: - Restricted preciseness and accuracy of the used balances to weight little amounts of potent medicine.
Solution: - Drug triturates -Suitable diluents like milk sugar are mixed with the potent drug to create ten - 20%w/w drug triturates.

Incompatible salts:
Problem: - With chemicals incompatible salts once triturated along turn out discoloration, chemical deterioration or loss of efficiency.
Solution: - Combining such substances with minimum pressure. Use a convenient methodology for admixture the powder like tumbling during a jar or spatulation on a sheet of paper.

II. CONCLUSION:

Mouth dissolving strips have gained quality due to higher patient compliance, fast drug delivery system, 1st pass metabolism and degradation in epithelial duct is avoided. And AN innovative drug delivery system for all the population teams, specifically geriatric, medical specialty patients and patients with swallowing difficulties. Mouth dissolving Strips also are having nice potential of delivering the medicative agent systemically yet domestically and have many benefits over several indefinite quantity forms. Today these granules are gaining a lot of importance in trade targeting medicine, gerontology and every one age teams. The ODGs have potential benefits over typical indefinite quantity forms, with their improved patient compliance; convenience, bioavailability and fast onset of action had drawn the eye of the many manufactures over a decade. Although sizable analysis has been tired the formulation development and technologies for FDGs, a lot of intensive investigations are to be dispensed during this promising space to end in newer efficient technologies and higher product. So the conclusion is ready on the premise of general analysis between the films and granules.

REFERENCES:

[1]. F. Cilurzo, I. E. Cupone, P. Minghetti, F. Selmin, L. Montanari, and Fast dissolving films made of maltodextrins, Eur. J. Pharm. Biopharm. 70 (2008) 895–900
[2]. J. Breitkreutz, M. Preis, M. Pein, Development of a Taste-Masked Orodispersible Film Containing Dimenhydrinate, Pharmaceutics 4 (2012) 551-562
[3]. M. Brown, V. Patel, F. Liu, Advances in oral transmucosal drug delivery, J. Controlled Release, 153 (2011) 106–116
[4]. P. Lakshmi, J. Sreekanth, A. Sridharan, Formulation development of fast releasing oral thin films of levocetrizinedihydrochloride with Eudragit® Epo and optimization through Taguchi orthogonal experimental design, Asian J Pharm 5 (2) (2011) 84-92
[5]. A. Amin, R. Mishra, Formulation and Characterization of Rapidly Dissolving Films of Cetirizine hydrochloride using Pullulan as a Film Forming Agent, Ind J Pharm Edu Res, 45 (1) (2011) 71-77
[6]. A. Arya, A. Chandra, V. Sharma, K. Pathak, Fast Dissolving Oral Films: An Innovative Drug Delivery System and Dosage Form, Int. J. ChemTech Research, 2 (1) (2010) 576583
[7]. K. Patel, S. Soni, R. Patel, V. Pandya, P. Bharadia, Mouth Dissolving Film: A Review, IJPRS 1 (3) (2012) 154-163
[8]. M. Panchal, H. Patel, A. Bagada, K. Vadalia, Formulation and Evaluation of Mouth Dissolving Film of Ropinirole Hydrochloride by Using Pullulan Polymers, IJPRAS 1(3) (2012) 60-72

[9]. S. Gauri, G. Kumar, Fast Dissolving Drug Delivery and Its Technologies, the Pharma Innovation 1 (2) (2012) 34-39
[10]. B. Bhyan, S. Jangra, M. Kaur, H. Singh, Orally Fast Dissolving Films: Innovations In Formulation And Technology, Int. J. of Pharm Sci Review and Research 9 (2) (2011) 5057
[11]. P. Dhere, S. Patwekar, Review On Preparation And Evaluation Of Oral Disintegrating Films, IJPT 3(4) (2011) 1572-1585
[12]. N. Giarratana, V. Reiner, N. Monti, A. Breitenbach, P. Klaffenbach, Rapidfilm ®: An Innovative Pharmaceutical Form Designed To Improve Patient Compliance, Int. J. Pharmaceutics 393 (2010) 55–60
[13]. N. Bhura, K. Sanghvi, U. Patel, B. Parmar, D. Patel, A Review On Fast Dissolving Film IJPRBS 1 (3) (2012) 66-89
[14]. M. D. NehalSiddiqui, G. Garg, P. K. Sharma, a Short Review on a Novel Approach in Oral Fast Dissolving Drug Delivery System and Their Patents, Advan. Biol. Res. 5 (6) (2011) 291-303
[15]. A. Waugh, A. Grant, Ross And Wilson Anatomy And Physiology in Health and Illness Ninth Edition, Churchill Livingstone Publication (2004) 289-293 16. J. O. Morales, J. T. McConville, Manufacture and characterization of mucoadhesivebuccal films, Eur. J. Pharm. Biopharm.
[16]. 77 (2011) 187–199
[17]. R. P. Dixit, S. P. Puthli, Oral strip technology: Overview and future potential, Journal of Controlled Release 139 (2009) 94– 107
[18]. S. Kalyan, M. Bansal, Recent Trends in the Development of Oral dissolving Film, International Journal of PharmTech Research 4 (2) (2012) 725-733
[19]. M. Dahiya,S. Saha, A. Shahiwala, A Review on Mouth Dissolving Films, Current Drug Deliv. 6 (5) (2009) 469-476
[20]. M. M. Gupta, M. G. Patel, M. Kedawat, Enhancement of dissolution rate of rapidly dissolving oral film of meclizine hydrochloride by complexation of Meclizine hydrochloride with ß-cyclodextrine, Journal of Applied Pharmaceutical Science 1 (9) (2011) 150-153
[21]. S. Thakur, Mouth Dissolving Films: A Review, Int J Pharm Bio Sci 4 (1) (2013) 899 – 908.
[22]. Pebley, WS, Rapidly disintegrating tablet, US patent, 1994, 5,298,261.
[23]. Koizumi, K, Watanabe, Y, Morita, K, Utoguchi, N and Matsumoto, M, New method of preparing high porosity rapidly saliva soluble compressed granules using mannitol with camphor, a subliming material,Int. J. Pharm., 152, 1997, 127-131.
[24]. Makino, T, Fast dissolving tablet and its production, US patent, 1998, 5,720,974.
[25]. Allen, LV and Wang, BM, Process for making a particulate support matrix for making rapidly dissolving tablet, US patent, 1996, 5,587,180.
[26]. Allen, L. V., Method for producing a rapidly dissolving dosage form, US patent, 2000, 6,066,337.
[27]. Ishikawa, T, Mukai, B, Shiraishi, S, Naoki, U, Makiko, F, Matsumoto, M and Watanabe, Y, Preparation and evaluation of granules rapidly disintegrating in saliva containing bitter taste-masked granules by the compression method, Chem. Pharm. Bull., 47(10), 1999, 1451-1454.
[28]. Bhaskaran, S and Narmada, GV, Indian Pharmacist, 1(2), 2002, 9-12.
[29]. Dor JM, Fix JA, Johnson MI. A new in vitro method to measure the disintegration time of a fast disintegration tablet. ProcIntSymp Control RelBioact Mater. 1999; 26: 939–940.
[30]. Makino T, Yamada M, Kikuta JI. Fast-dissolving tablet and its production. US Patent 5,720,974. 1998 Feb 24.
[31]. Valleri M, Mura P, Maestrelli F, Cirri M, Ballerini R, Development and evaluation of glyburide fast dissolving granules using solid dispersion technique. Drug Dev Ind Pharm, 30 (5): 525-534, (2004).
[32]. Sastry SV, Nyshdham JR, Fix JA. Recent technological advances in oral drug delivery: A review. Pharmaceutical Science and Technology Today. 2000
[33]. 33:138-45. 3. Seager H. Drug-delivery products and the Zydisfastdissolving dosage form. Journal of Pharmacy and Pharmacology. 1998; 50(4):375-82.
[34]. Fu Y, Yang S, Jeong SH, Kimura S, Park K (2004). Orally fast disintegrating granules: Developments, technologies, taste masking and clinical studies. Crit Rev Ther Drug Carrier Syst21: 433–76.
[35]. Tejvir Kaur at all and co. a Review article an Month dissolving granules published in

international journal of current pharmaceutical research in vol-3; issue-1-2011.
[36]. Brown D (2001). Orally disintegrating granules: Taste over speed. Drug DelivTechnol 3: 58-61.
[37]. Mrs. RajeshreePanigrahi at all and co a review article on fact dissolving granules published in webl medcentral.com; article ID-Wmc00809; 29-sep- 2010.
[38]. Patel.H A, Patel J.K, Patel K.N and Patel R.R. Studies on formulation and in vitro evaluation of fast dissolving granules of domperidone. Indian J Pharm Sci, 2010; 2 (1):470-476.
[39]. ChackolA.j, Josel S, Babul N, Michellel M, Design and Development of Orodispersible granules of Promethazine Theoclate Using CoprocessedSuperdisintegrants and Subliming Materials, International Journal of Innovative Pharmaceutical Research, 1(2), 2010, 53-56.
[40]. Dobetti L, Fast disintegrating granules, US Patent 2003, 6:596, 311.
[41]. 41.https://www.slideshare.net/mftrj1993/pharmaceutical-granules.
[42]. Arun A, Amrish C, Vijay S, Kamla P (2010) Fast dissolving oral films: an innovative drug delivery system and dosage form. Int J Chem Tech Res 2(1):576–583
[43]. Aulton ME, Wells TI (1988) Pharmaceutics: the science of dosage form design. Churchill Livingstone, London Banker GS, Anderson NRI (1987) Tablets. In: Lachman L, 44.LiebermanHA,KanigJL(eds)Thetheoryandpracticeofindustrialpharmacy, 3rd edn. Varghese Publishing House, Mumbai, pp 293–299
[44]. Bystolic [package insert]. St. Louis, MO: Forest laboratories, Inc. (2007)
[45]. Chouinard J (2000) Dysphagia in Alzheimer disease: a review. J Nutr Health Aging 4(4):214–217
[46]. 47.Deepthi A, Venkateswara RB, Navaneetha K (2014) Formulation and evaluation of fast dissolving oral films of zolmitriptan.
[47]. AJADD 2:153–163 48.Dinge A, Nagarsenker M (2008) Formulation and evaluation of fast dissolving films for delivery of triclosan to the oral cavity. AAPS PharmSciTech 9(2):349–356
[48]. 49.Dixit AS, Parthasarathi KK, Hosakote GS (2011) Gels and jellies as a dosage form for dysphagia patients: a review. Curr Drug Ther 6:79–86
[49]. Siddiqui N, Garg G, Sharma P. A Short Review on "A Novel Approach in Oral Fast Dissolving Drug Delivery System and Their Patents. Advances in Biological Research, 2011; 5(6): 291-303.
[50]. Patel VF, Liu F, Brown M. Advances in Oral Transmucosal Drug Delivery. Journal of Controlled Release, 2011; 153: 106– 116.
[51]. Panigrahi R, Behera S, Panda C. A Review On Fast Dissolving Tablets. Webmed Central Pharmaceutical Sciences, 2010; 1(11): 1-15.
[52]. Bandari S, Mittapalli RK, Gannu R, et al. Orodispersible tablets: An overview. Asian J Pharm, 2008; 2: 2-11.
[53]. Hearnden V, Sankar V, Hull K, et al. New developments and opportunities in oral mucosal drug delivery for local and systemic disease. Advanced Drug Delivery Reviews, 2012; 64: 16-28.
[54]. Dixit RP, Puthli SP, Oral strip technology: Overview and future potential. Journal of Controlled Release, 2009; 139: 94–107.
[55]. Cilruzo F and Cupone EI: Fast dissolving films made of maltodextrins. European Journal of Pharmaceutics and Biopharmaceutics, 2008; 70: 895-900.