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A Review Of Mouth Dissolving Tablet Formulations Using Various Cosolvents.

1Sejal Pravin Kadam, 2Anwesha Lovlin Garnaik

1Pharmacy final year

1Mumbai university

Abstract:

Mouth dissolving tablets are those tablets which when placed in mouth get dissolved rapidly in saliva without the need of liquid and can be swallowed. Conventional dosage form such as tablets and capsules are the most popular among all dosage forms existing today because of its convenience of self adminstration, compactness and easy manufacturing. To overcome these problems, mouth dissolving tablets have been developed, which having a good hardness, dose uniformity, easy administration and serves as a first choice of dosage forms for pediatrics, geriatrics and travelling patients. Some tablets are designed to dissolve in saliva remarkably fast,within a few seconds,and are true fast dissolving tablets. This tablets format is designed to allow adminstration of an oral solid dose form in absence of water or fluid intake.Such tablet readily dissolve or disintegrate in saliva generally within < 60 seconds.

KEY WORDS : pholorogucinol, mouth dissolving tablets,cosolvents, experimental design, disintegrate, fast dissolving traditional dosage form.

INTRODUCTION:

Mouth dissolving tablets “The mouth dissolving are defined as the solid dosage forms that rapidly get disintegrate and dissolve into saliva in oral cavity, results into solution without the need of water for administration.[1] Solid dosage forms are popular because of ease of administration of accurate dose ,self medication, avoid pain and most importantly the patient compliance.[2] The mouth dissolving tablets are also known as the fast melting tablet or fast dispersing tablet, rapid melt tablet, freeze dried wafers and quick disintegrating tablets.[1,2]. The most popular solid dosage form are beings as tablets and capsules. Oral drug delivery most preferred as route of administration which have wide acceptance upto 50-60% of total dosage forms [3].

Mouth dissolving tablets (MDT) have been developed, which having a good hardness and dose uniformity, easy to administration and servers as the first choice of dosage form for pediatrics , geriatrics and travelling patients.[5] The mouth dissolving tablets is regarded as one of the most cutting-edge approaches to oral medication delivery fast dissolving tablets are novel drug delivery systems that dissolves, disintegrate or disperse the Active Pharmaceutical Ingredients in saliva. Fast dissolving tablets are a novel drug delivery systems that dissolves, disintegrate or disperse the API in saliva within few seconds with or without intake of water.[4] The FDA formulation is defined by the Food and Drug Administration [(FDA) as " a solid dosage form containing medical substances which disintegrates rapidly, usually within a seconds ,when placed upon the tongue.[1 2 4] The tablets disintegrate into smaller granules or melt in the mouth

from a hard solid structure to gel like structure ,allowing easy swallowing by the patients. [8]

Mouth dissolving tablets (MDT s) have been proposed as a novel approach to avoid the first pass effect and enhance the bioavailability of drugs .[7] Among the several methods used for manufacturing MDTs ,as direct compression seems to be preferable one due to the limited number of processing steps ,the low manufacturing cost and conventional equipment used.[6 ,7]

Pholorogucinol (PHL) is the nootropic derivative with marked antispasmodic properties.

Pholorogucinol (1,3,5-trihydroxybenzene) is effective, well-tolerated antispasmodic agents, widely known in word, registered for the therapy of renal and biliary colic. 1,3,5 l- trimethoxybenzene has antispasmodic effect [1]

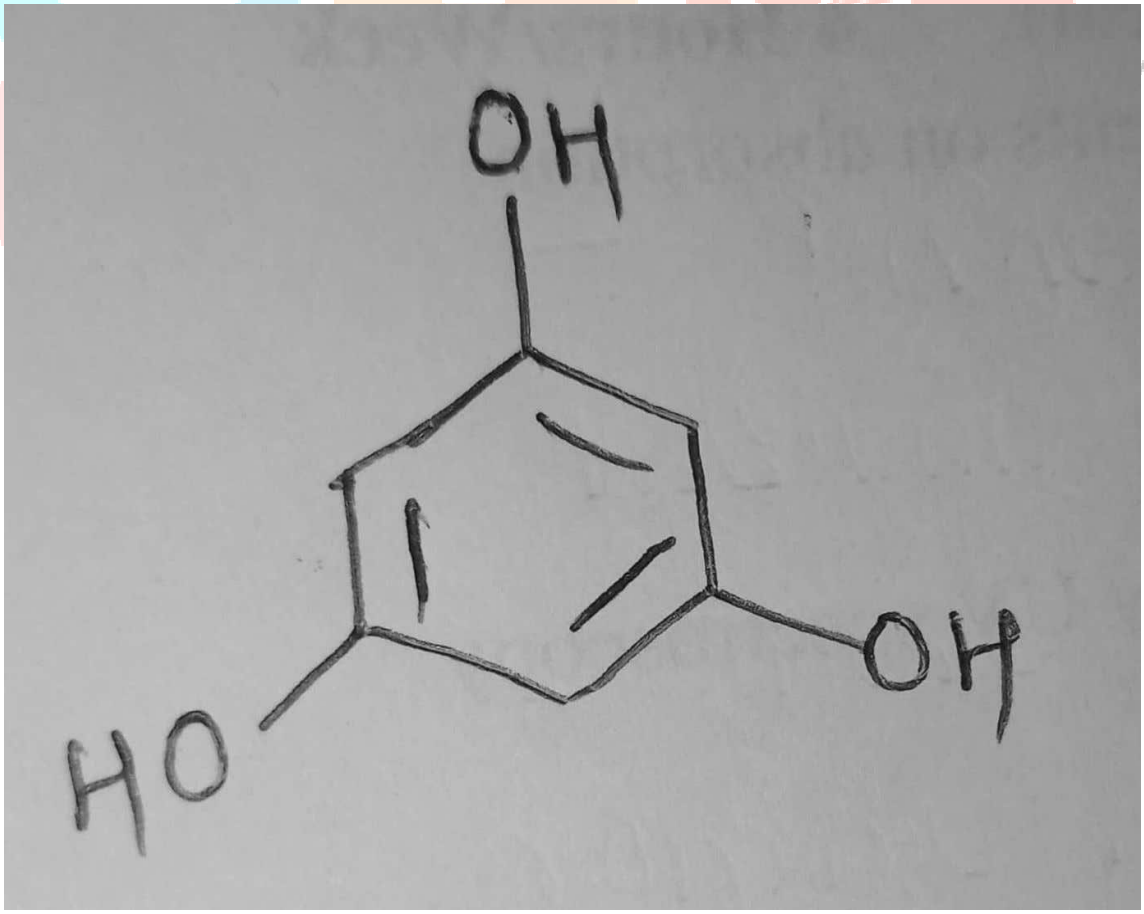

Fig 01 CHEMICAL STRUCTURE OF PHOLOROGUCINOL

Pholorogucinol and it's methylated derivative are antispasmodic agents acting on smooth muscle. Pholorogucinol treating abdominal pain verbs placebo. [9] Pholorogucinol is a musculotropic anti-spasmodic drug.Its frequency prescribed in many European countries with a considerable cost for health services. [12]

Pholorogucinol is commonly used to alleviate dysmenorrhea and stomach cramps. The effects of pholorogucinol of the contraction of rat gastric circular muscles and uterine smooth muscle induced by oxytocin (OT) were investigated. [11] The main tactic is to produce mouth dissolving or mouth dissolving tablets that , because the superb disintegrates in the formulation, dissolving rapidly in saliva in matter of second without need for water .[10, 11]

MOUTH DISSOLVING PHENOMENON:

All mouth dissolving tablets approved by a FDA is an classified as orally disintegrating tablets

Mouth dissolving tablets, also known as a orally disintegrating tablets (ODT,S) are solid oral dosage forms that disintegrate or dissolve rapidly in mouth typical within seconds, without needing water.

These pholorogucinol tablets are developed to o rapid action and improve patient compliance for antispasmodic drugs pholorogucinol by offering convenient, fast acting opens for mangling condition like acute spasms.

Bioavailability of a drug depends in absorption of the drug, which is affected by solubility of drug in gastrointestinal fluid and permeability of the drug across gastrointestinal members.

MECHANISM OF ACTION: (flow chart 15 16)

- **Swelling** : saliva in the mouth causes the disintegration agent to swell, creating channels for the saliva.
- **Porosity and capillary action (wicking):** Disintegration by capillary action is always the first step. This type of disintegrate facilities the breakdown of a tablet by drawing water into the matrix through capillary action.

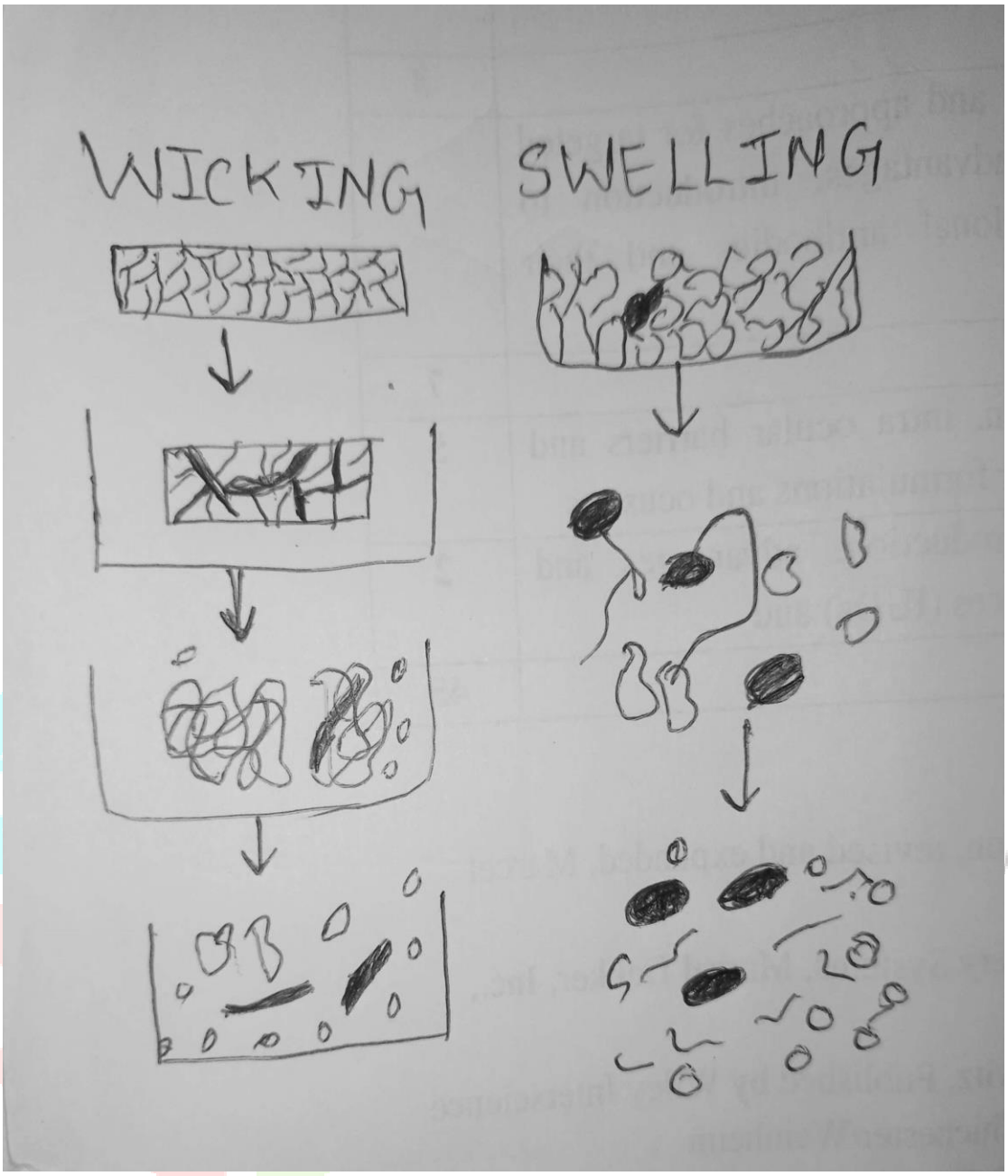

Fig 02 PROCESS OF WICKING AND SWELLING [28]

- **Due to disintegrating particle / particle repulsive forces**: No swelling particles also cause disintegration of tablets, helps break down non – swellable disintegrates.

- **Due to deformation :** During compression, disintegrated particles get deformed and these deformed particles get into normal structure when they come in contact with aqueous media or water.

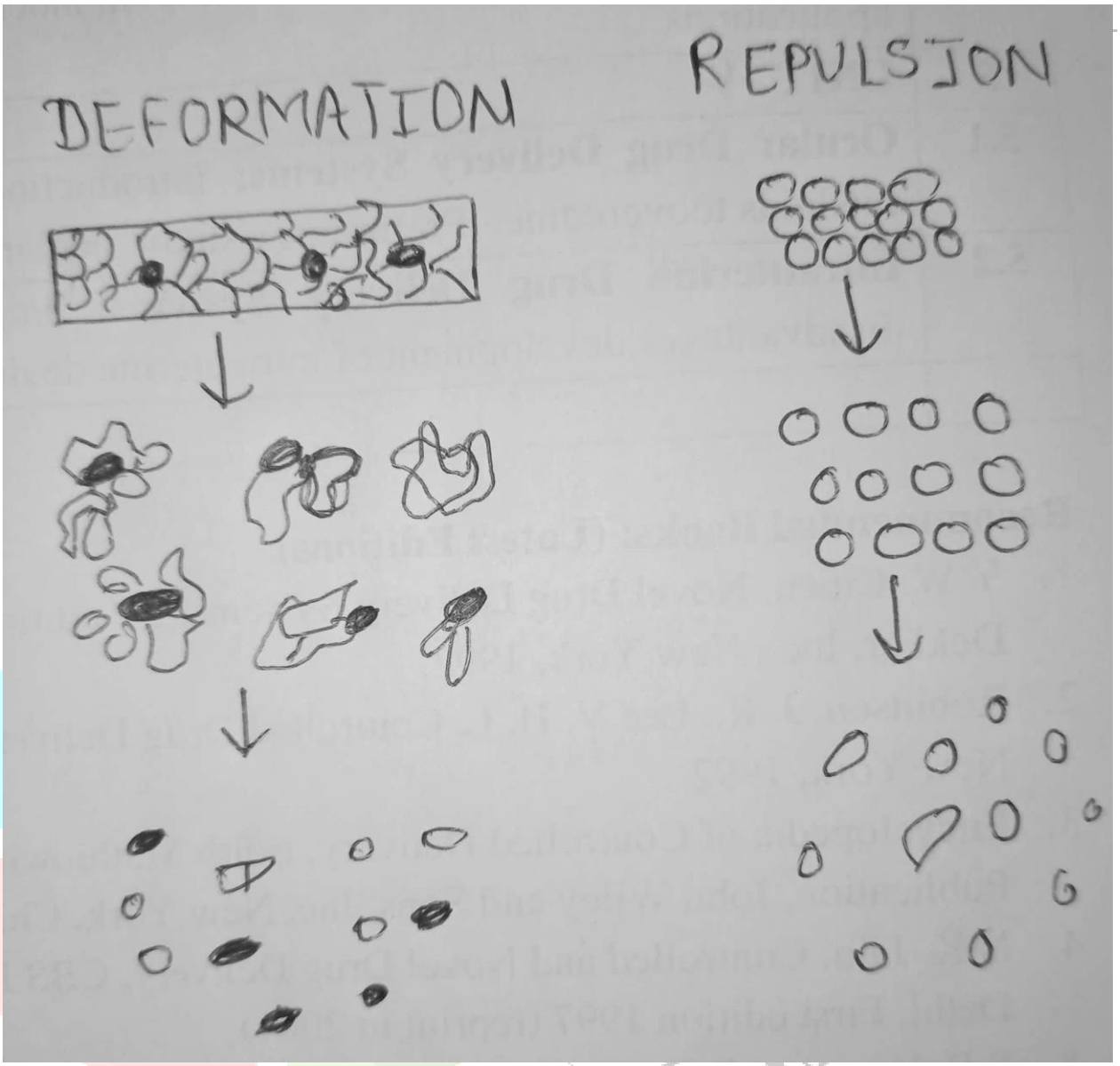

FIG 03 PROCESS OF DEFORESTATION AND REPULSION [28]

IDEAL CHARCTERISTICS OF MOUTH -DISSOLVING TABLET,:

1. Have a pleasantly mouth feel
2. Be harder and less friable
3. Not required water to swallow to tablets [15]
4. Easily dissolving/ disintegrating in saliva within few seconds
5. Exhibit low sensitivity to environment condition.[17]
6. Allow high drug loading.
7. Leave minimal or no residue in the mouth after oral administration. [18]

POTENTIAL DRUGS CANDIDATES ARE A MOUTH DISSOLVING TABLET :[13]

- **NSAID's :** Paracetamol, Ibuprofen
- **ANTI-HISTAMINC DRUGS:** Meclizine , Loratadine
- **ANTI ULCER DRUGS** : Famotidine , Lansoprazole
- **ANTI-PARKINSION DRUGS :** Selegiline
- **ANTI-EMETIC DRUGS:** Ramosetoron HCL , Ondansetran.

ADVANTAGES :

1. Good mouth feel property of MDDDS helps to change the basic view of medications of drugs.
2. Pregastric absorption can result in improved bioavailability, reduced dose and improved clinical performance by reducing side effects [15, 19]
3. Effective in lower concentrations.
4. It's biodegradable .
5. Does not stick to punches and dyes.[2]
6. Bioavailability of drugs is enhanced due to absorption from mouth ,pharynx and esophagus.

DISADVANTAGES:

1. The tablets may taste bad and feel grainy in the mouth if they are not prepared properly.
2. Convenient to administer specially for geriatric , pediatrics,mentally disabled and bed ridden patients who have difficulty in swallowing [8]
3. To maintain maximum stability and product security, mouthwash pills require special packaging [20]
4. Because they are hygroscopic , MTD's must be keep in dry environment [13]
5. If the pills are not prepared correctly, they may have a poor taste and feel gritty in the mouth.

INGREDIENTS USED IN MOUTH DISSOLVING TABLETS:

-It's helps in quick release of drug.

-Result in faster dissolution.

INGREDIENTS TYPES:	ROLE OF INGREDIENTS	EXAMPLES	REFERENCE
Super-disintegrating	Burst disintegration facilitator. To ensure quick disintegrating and high dissolution rate. Promotes the wettability and dispensability of the system , thus enhancing the disintegration and dissolution.	Sodium starch glycolate,Ac-di-sol(Crosscarmellose sodium), Crospovidone, Microcrystalline cellulose.	5 ,23,24,25.
Flavours (Used as sweeteners)	Flavours and taste masking agents make the products more palatable and pleasing for patients.	Peppermint flavour,cooling flavor, and flavor Oil.	5
Binders	Binders keep the composition of these fast-melting tablets together during the compression stage. Maintain the integrity and stability of the tablets.	Polyvinyl pyrrolidone,Polyvinyl alcohol, Hydroxyl propyl methyl cellulose.	26,5
Fillers	Compressibility and Disintegration	Mannitol, Sorbitol, Xylitol , Calcium carbonate, Magnesium carbonate.	25

Emulsifier	Disintegration accelerator. Bioavailability enhancer of immiscible substances.	Sodiumdoecylsulfate, Sodium lauryl sulfate,polyoxyethylene sorbitan fatty acid esters(Tweens)	21 , 27
Lubricants	Assists in making these tablets more palatable after they disintegrate in mouth.	Stearic acid, Magnesium stearate, Zinc state , Calcium State, Talc, Polyethylene	5

TECHNIQUES OF PREPARING MOUTH DISSOLVING TABLETS:

-They are many techniques involved:

1. Freeze -Drying or Lyophilization:

-A Process in which water is sublimated from the product after freezing.

Lyophilization is a pharmaceutical technology which allows drying of heat sensitive drugs and biological at low temperature under conditions that allow removal of water by sublimation [1,13]. Lyophilization results in preparation, which are highly porous, with a very high specific surface area, which dissolve rapidly and show improved absorption and bioavailability.High cost of equipment and processing limits the use of this process [29].

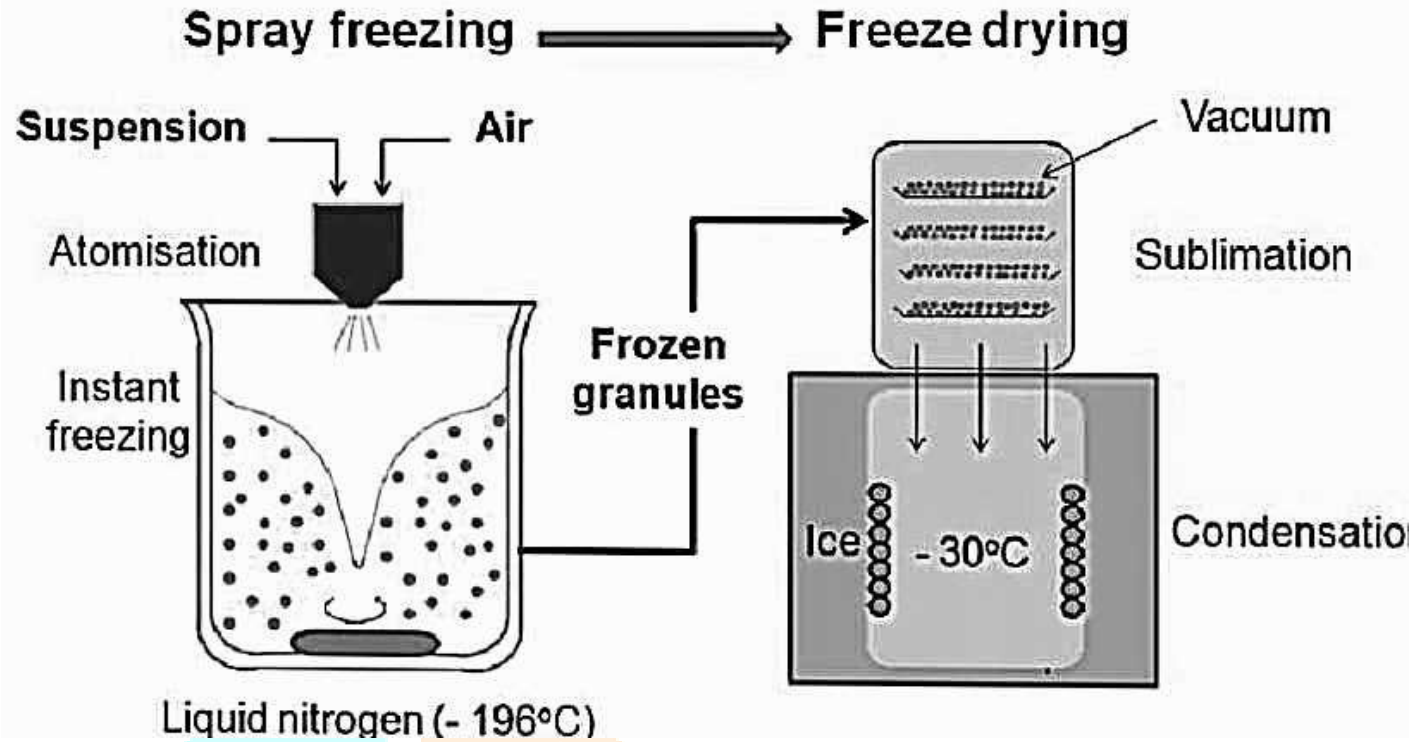

FIG 04 PROCESS OF FREEZE DRYING TECHNOLOGY [30]

2. Molding:

-There are two types of molding process i.e. solvent method and heat method.solvent method involves moistening the powder blend with a hydro – alcoholic solvent followed by compression at a low pressure in molded plates to form a wetted mass (compression molding) Air – drying is done to remove the solvent [28] .The tablets manufactured so formed are less compact than compressed tablets and posses a porous structure that hastens dissolution. In the heat molding process a suspension is prepared that contains a drug, agar and sugar (e.g.mannital or lactose).This suspension is poured in the blister packaging wells and then agar is solidified at the room temperature to form a jelly and dried at 30°C under vacuum. The main concern about these molded tablets is their mechanical strength,which can be achieved by using binding agents [31]

The spray congealing of a molten mixture of hydrogenated cottonseed oil, sodium carbonate, lecithin, polyethylene glycol and an active ingredient into a autoes based tablet triturate form was used to prepare the taste masked drug particles. As compared to the Lyophilization form was used to prepare the taste masked drug particles. As compared to the Lyophilization technique. Tablets produced by the molding technique are easier to scale up for industrial scale manufacturing.

3.Sublimation:

The process involves addition of some inert volatile substance like urea, urethane, naphthalene , camphor ,etc. to other excipients and compression of blend structure, due to which tablet dissolves when comes in contact with saliva. Additional several solvent like cyclohexene, benzene etc. can also be used as pore forming agents. Mouth dissolving tablets with highly porous structure and good mechanical strength have been developed by this method.[28,31,32]

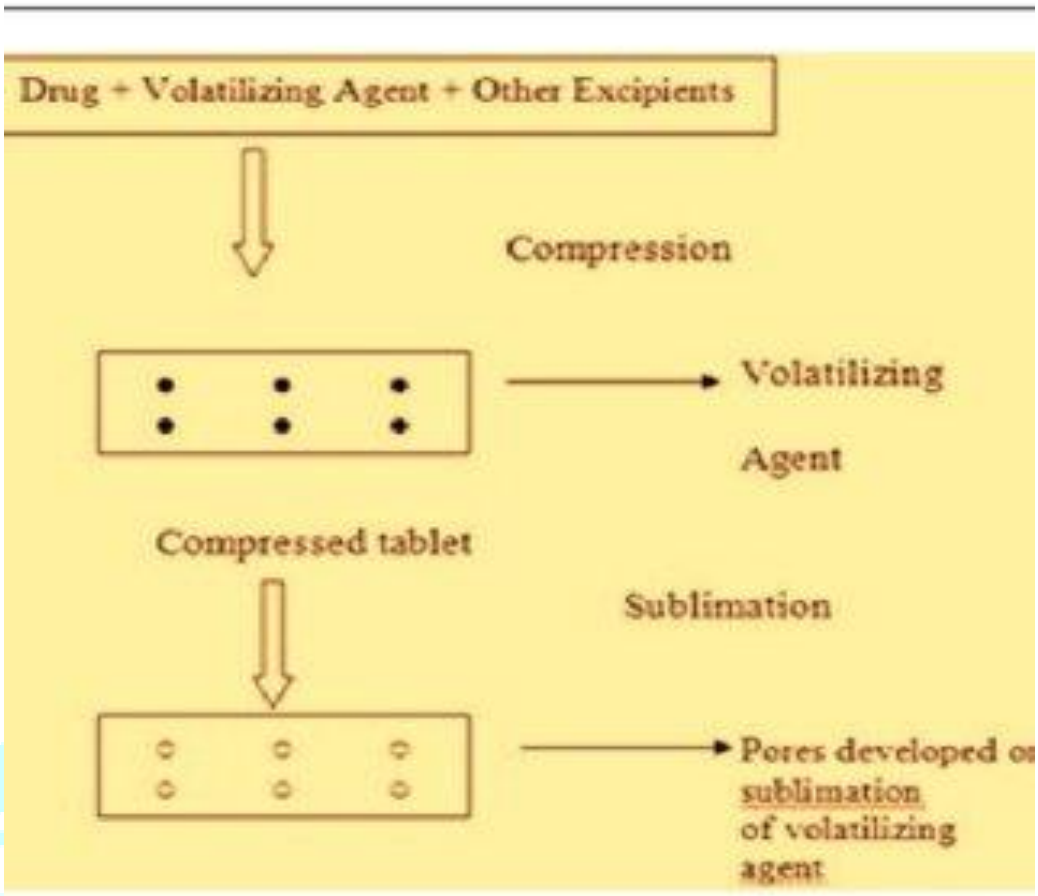

Fig 05 SUBLIMATION PROCESS BY MDTs [28]

4.Spray drying technology:

To produce extremely porous powders, the pharmaceutical sector use spray-drying technology. The processing solvent quickly Evaporates as a result of spray-drying, leaving behind a highly porous product that can be used to make delectable tablets.

It has been observed that tablets made from the spray-drying powder dissolve in aqueous solution<20. [13]

5.Dircet compression method:

One of the most widely used methods for creating mouth- dissolving tablets is the disintegrate addition approach, which is inexpensive and excipients mixes,without any prior processing.

It's delivers excellent efficiency and has advantages over other tablets production methods like a

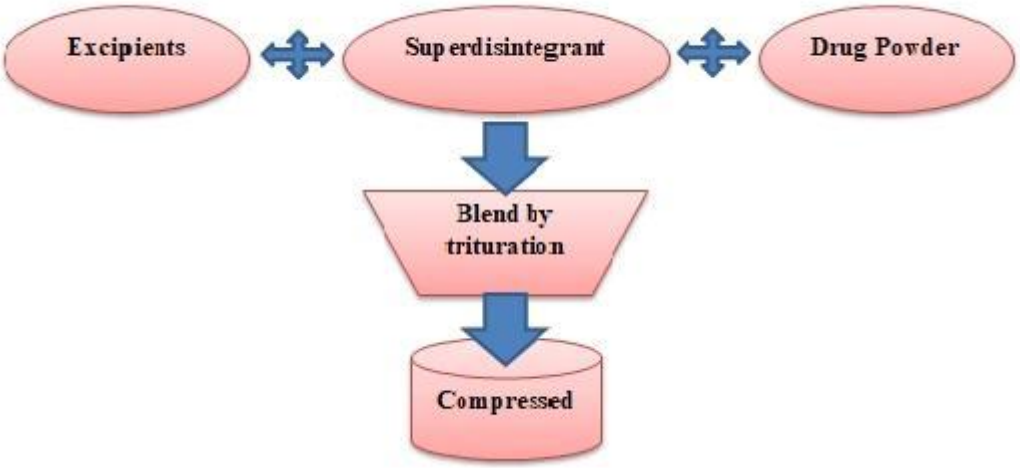

Fig 06 DIRECT COMPRESSION TECHQIUES [4]

wet granulation [4,34] The mixture that is to be a compressed need to flow properly and cohere under pressure. Adding super disintegrations in the right concentration to provide fast Disintegration and a pleasantly mouthfeel is the fundamental idea behind creating mouth- dissolving tablets using a disintegrating addition approach [33]

FORMULATION STEPS FOR PHOLOROGUCINOL MOUTH DISSOLVING TABLETS USING A COSOLVENT METHODS:

Excipients	Ingredients	Role
1. **API (Active pharmaceutical ingredients)**	Pholorogucinol drug	Balancing it's solubility enhancement with biocompatibility and safety for the final product.[35,36]
2. **Fillers and sweeteners**	Mannitol	Mannitol is non sticky and crystalline , contributing to a smooth texture that is highly desirable for a oral applications. Enhancing mouthfeel and taste. Mild sweeteners [36,37]

3. **Stabilizer**	Citric acid	Enhancer, helps stabilizer the drug. Proper improving the flavor taste of tablets
4. **Binder**	Providone k 30	Dissolved in the cosolvents blends properly.[34]
5. **Super disintegrations**	Sodium starch glycolate (SSG)	Helps aids tablets break-up.
6. **Lubricants**	Magnesium stearate	It's prevents sticking during compression.

STEPS OF FORMULATION PROCESS:

- Choose proper cosolvents and excipients
- Prepare the binder solution
- Mix and slurry the powder
- Granulation and drying process
- Compression and lubricants

EVULATION OR QUALITY CONTROL TEST :[15]

1. General appearance – The general appearance of a tablet, it's visual identity and over all "elegance" is essential for a customer acceptance.

2. Size and shape : The size and shape of tablets can be dimensionally , monitored and controlled.

3. Weight variation : 20 tablets were selected randomly from the lot and weighted individually to check for weight variation.

4. Hardness and friability of tablets : The strength of tablet is expressed as tensile strength (kg/cm2)

5. Wetting time and Water absorption ratio: A study on wetting time and water absorption ratio reported the use of a piece of double folded tissue paper placed in a petridish containing 6 ml of water.

6. Disintegration test : The Disintegration time of MDTs is measured using the disintegration test for conventional tablets that described in pharmcopoeias.

Conclusion:

When it comes to pharmaceuticals , mouth dissolving tablets are now more popular on the market than traditional dosage form like tablets and capsules.[13] Mouth dissolving tablets have potential advantages over conventional dosages forms, with their improved patient compliance, convenience, bioavailability and rapid onset of action has drawn the attention of many manufacturers over a decade.[1] The tablets produced with a new manufacturing technology have a quicker start of action , higher bioavailability,fewer side effects and improved safety. According to summary , individuals with dysphasia may benefit from MDT , which would increase their bioavailability.[13 ,7]

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