JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

FORMULATION AND EVALUTION OF ORAL DISPERSIBLE TABLETS

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ABSTRACT
Oral dispersible tablets (ODTs) are patient friendly dosage form that rapidly disintegrate or dispersed in mouth no the need of water. Developed ODTs were studied for their physicochemical properties and in vitro drug release profile. Thus, oral dispersible tablets are solid unit dosage forms like conventional tablets, but are composed of super disintegrants, which help them to dissolve the tablets within a minute in the mouth in the presence of saliva without any difficulty of swallowing. the most common method of preparation is the compression method. Other special methods are molding, melt granulation, phase-transition process, sublimation, freeze-drying, spray-drying, and effervescent method. Since these tablets dissolve directly in the mouth, so, their taste is also an important factor. Oral dispersible tablets are also called as orally disintegrating tablets, mouth-dissolving tablets, rapid-dissolving tablets, fast-disintegrating tablets, fast-dissolving tablets. The faster the drug into solution, quicker the absorption and onset of clinical effect.

Introduction
The most popular solid dosage forms are being tablets and capsules, one important drawback of this dosage forms for some patients, is the difficulty to swallow. Drinking water plays an important role in the swallowing of oral dosage forms. Often times people experience inconvenience in swallowing conventional dosage forms such as tablet when water is not available, in the case of motion sickness (kinetosis) and sudden episodes of coughing during the common cold, allergic condition and bronchitis. For these reason, tablets that can rapidly
Dissolve or disintegrate in the oral cavity have attracted a great deal of attention.

Definition of ODT
ODT as a solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue. The significance of these dosage forms is highlighted by the adoption of the term Oral dispersible Tablet by the European Pharmacopoeia which describes it as a tablet that can be placed in oral cavity where it disperses rapidly before swallowing.

Criteria for Oral dispersible tablets
The tablets should
- Not require water to swallow, but it should dissolve or disintegrate in the mouth cavity.
• its should Be compatible with mouth cavity.
• its should Be portable without fragility concern in mouth cavity.
• its should Have a pleasant mouth feel.
Its should Leave minimum or no residue in the mouth after oral administration.
• its should be Exhibit low sensitive to environmental condition as temperature and humidity.
• its should be manufacture cost

Advantages of Oral dispersible tablets
• Administration to the patients, who can not swallow Such as pediatric, geriatric
• Rapid drug therapy intervention.
• Achieve increased bioavailability.
• Good mouth feel property helps to change the perception of medication as bitter pill
Particularly in pediatric patients.
• The risk of chocking or suffocation during oral administration of conventional
• Formulations due to physical obstruction is avoided, thus providing improved safety.
• New business opportunity like product differentiation, product promotion, patent
• Extension and life cycle management.
• No chewing needed
• need a Better taste
• Improved stability
• Allows high drug loading.
• Ability to provide advantages of liquid medication in the form of solid preparation.
• Cost- effective for patients.

Disadvantages of Oral dispersible tablets
These are highly hygroscopic, so care has to be taken while storage.

• Drugs with relatively larger doses are difficult to not formulate into ODTs like. antibiotics.
• Due its porous structure ODTs are highly fragile sometimes.
• ODTs require special packaging for proper stabilization & safety of stable product.
• After taking ODTs special precautions must be taken, like eating and drinking may become restricted for some time.

Ideal properties of Oral dispersible tablets

Not require water to swallow and should dissolve or disintegrate in the mouth within a few seconds
• High drug loading
• Be compatible with taste masking and other excipients
• Have a pleasing mouth feel
• Leave minimal or no residue in the mouth after oral administration
• Exhibit low sensitivity towards environmental conditions such as humidity and temperature
• Be adaptable and amenable to existing processing and packaging machinery.
Preparation and packaging must be done through conventional methods.

Challenges in the Formulation of Oral dispersible tablets

Mechanical strength and disintegration time
Taste masking
Disintegration pattern and additives
Aqueous solubility
Size of tablets
Amount of drug
Hygroscopicity
Mouth feel
Good packaging design
Sensitivity to environmental conditions
Cost

Various Techniques Used In Preparation of Oral dispersible Tablets Conventional technologies

Freeze Drying or Lyophillization
Tablet molding
Direct compression
Spray drying
Sublimation
Mass extrusion

General excipients used in oral dispersible tablet

Superdisintegrants (SDS)

Disintegrating agents are substances routinely included in the tablet formulations to aid in the break-up of the compacted mass into the primary particles to facilitate the dissolution or release of the active ingredients when it is put into a fluid environment. The major function of disintegrants is to oppose the efficiency of the tablet binder and physical forces that act under compression to structure the tablet. Recently new material termed as superdisintegrants" have been developed to improve the disintegration processes.

Selection of Superdisintegrant

The requirement placed on the tablet disintegrants should be clearly defined.
The ideal disintegrants should have-
1) Poor solubility.
2) Poor gel formation.
3) Good hydration capacity.
4) Good moulding and flow properties.
5) No tendancy to form complexes with the drugs.
6) Good mouth feel.
7) It should also be compatible with the other excipients and have desirable tableting properties.

Advantages of Superdisintegrants

1) Effective in lower concentrations than starch.
2) Less effect on compressibility and flow ability.
3) More effective intragranularly.

Mechanism of Superdisintegrants

Superdisintegrants are used to improve the efficacy of solid dosage forms.
Swelling
Porosity and capillary action (Wicking)
Heat of wetting
Chemical reaction (Acid-Base Reaction)
Particle repulsive forces
Deformation recovery
By enzymatic reaction

Classification of superdisintegrants on the basis of origin.

Synthetic Superdisintegrants	Natural Superdisintegrants
Starch	Pectin
Modified Starch	Agar
Cross-linked PVP	Veegum
Cross-linked sodium CMC	Bentonite
Sodium Starch Glycolate	Ion exchange Resin (Indion 414)
Sta RX 1500 (Pregelatinized Starch)	

Various commercially available superdisintegrants along with their properties.

Superdisintegrants	Nature	Properties	Mechanism
Crosspovidone	Crosslinked homo polymer of *N*-vinyl-2-pyrrolidone	Particle size - 100 µm, insoluble in water, gives smoother mouth feel	Both swelling and wicking
Cross carmellose sodium	Cross-linked form of sodium CMC	Particle size 200 mesh, insoluble in water	Swelling
Sodium starch glycolate	Crosslinked low substituted carboxymethyl ether of poly-glucopyranose	Particle size 140 mesh, insoluble in organic solvents, disperses in cold water and settles in the	Water uptake followed by rapid and enormous swelling

		form of a highly saturated layer	
Acrylic acid derivatives 43 (Yang *et al*. 2004)	Poly(acrylic acid) super porous hydrogel	Particle size 106 µm, DT-15 + 2 S	Wicking action
Effervescent mixture	Citric acid, tartaric acid, sodium bicarbonate	Crystalline nature	Effervescence
Sodium alginate	Sodium salt of alginic acid	Slowly soluble in water, hygroscopic in nature	Swelling
NS-300 43 (Ozeki *et al.* 2003	Carboxy methyl cellulose	Particle size 106 µm, DT - 20 S	Wicking type
ECG-505 43 (Ozeki *et al*. 2003)	Calcium salt of CMC	Particle size 106 µm, DT - 80S	Swelling type
L-HPC 43 (Ozeki *et al.* 2003)	Low hydroxy propyl cellulose	Particle size 106 µm, DT-90S	Both swelling and wicking

Factors Affecting Disintegrants Activity

1.Particle size
2. Molecular Structure
3. Effect of compression force
4. Matrix Solubility
5. Method of Incorporation in Granulation
6. Effect of Reworking
   7 Binder
   8 Diluents
   9 Lubricants
   10 Glidants

Taste Masking

The drugs are mostly bitter in nature. Taste masking is needed to hide the bitter taste in ODTs formulations which can be achieved by using combination of right flavour and right sweeteners.

An ideal taste masking process and formulation should have the following properties.

- Involve least number of equipment's and processing steps
- Require minimum number of excipients for an optimum formulation.
- No adverse effect on drug bioavailability.
- Require excipients that are economical and easily available.
- Least manufacturing cost
- Require excipients that have high margin of safety
- Rapid and easy to prepare

Physiology of taste
Taste Masking Technologies
Use of flavor enhancers
Coating of drug particles with inert agents
Solid dispersion system
Microencapsulation
Multiple emulsions
Using liposome

Drugs Eligible for Oral dispersible Tablet's

The eligibility criteria for drugs to be formulated as Fast Dissolving Tablets are low dose, good stability in aqueous media, and good mechanical strength hand compatibility with excipients.

Class of Drug	Drug
Analgesic/Anti-inflammatory Agents	Picroxicam, Ibuprofen, Mefenamic Acid
Anti-Bacterial Agents	Erythromycin, Tertacycline, Doxycycline, Rifampin
Anti-Emetic	Ondansetrone, Dolasetron, Granisetron, Promethazine
Anti-Fungal	Griseofulvin, Miconazole
Anti-Malarial	Chlorquine, Amodiaquine
Anti-Gout	Allopurinol, Probenecid
Anti-Hypersentive	Amlodipine, Nefidipine
Anti-Coagulants	Glipizide, Tolbutamide
Anti-Protozoal	Benznidazole, Tinidazole
Anti-Thyroid	Carbimazole
Cardiac Inotropic Agents	Digitoxin, Digoxis
Corticosteroids	Prednisolone, methylprednisolone, hydrocortisone, betamethasone, prednisone, dexamethasone

Local anaesthetics	Lidocaine
Gastro-Intestinal Agents	Omeprazole, Ranitidine, Famotidine
Nutritional Agents	Vitamin A, Vitamin B, Vitamin D, etc
Oral Vaccines	Influenza, Hepatitis, Polio, Tuberculosis, etc.

Excipients and Materials used oral dispersible tablets

Sr. No.	Materials used	Category
	Active pharmaceutical ingredient	Active Ingredient
	Sodium Starch Glycolate	Super disintegrant
	Crospovidone	Super disintegrant
	Crosscarmellose Sodium	Super disintegrant
	Microcrystalline Cellulose	Diluents
	Aspartame	sweetener
	Mannitol	sweetener
	Talc	Glidant
	Pineapple Flavor	Flavor
	Magnesium Stearate	Lubricant

Croscarmellose sodium

- Non-proprietary Name:
  - BP : Croscarmellose sodium
  - Ph Eur : Carmellosum natrium conexum
  - USP-NF : Croscarmellose sodium
- Synonyms:

Ac-Di-Sol; crosslinked carboxymethylcellulose sodium; Explocel; modified cellulose gum; Nymcel ZSX; Pharmacel XL; Primellose; Solutab; Vivasol.

- Chemical Name and CAS Registry Number:

Cellulose, carboxymethyl ether, sodium salt, crosslinked and [74811-65-7]

- Empirical Formula and Molecular Weight:

Croscarmellose sodium is a crosslinked polymer of carboxymethylcellulose sodium and 90,000–7,00,000.

- **Functional Category:**

Tablet and capsule disintegrant.

- **Applications in Pharmaceutical Formulation or Technology:**

Croscarmellose sodium is used in oral pharmaceutical formulations as a disintegrant for capsules, tablets. In tablet formulation croscarmellose sodium may be used in both direct-compression and wet-granulation processes. Croscarmellose sodium at concentrations up to 5% w/w may be used as a tablet disintegrant.

- When used in wet granulations, the croscarmellose sodium should be added in both the wet and dry stages of the process (intra- and extragranularly) so that the wicking and swelling ability of the disintegrant is best utilized.

Crospovidone

- **Non-proprietary Name**:
  - BP : Crospovidone
  - PhEur : Crospovidonum
  - USPNF: Crospovidone
- **Synonyms :**

Crosslinked povidone; E1202; Kollidon CL; Kollidon CL-M; Polyplasdone XL; Polyplasdone XL-10; polyvinylpolypyrrolidone; PVPP; 1-vinyl-2-pyrrolidinone homopolymer.

- **Chemical Name and CAS Registry Number:**

1-Ethenyl-2-pyrrolidinone homopolymer and [9003-39-8]

- **Empirical Formula and Molecular Weight**

$(C_6H_{10}O_5)$ n 50, 000–1, 60, 000, Where n = 300–1000.

- **Functional Category:**

Tablet disintegrant.

- **Applications in Pharmaceutical Formulation or Technology**

Crospovidone is a tablet disintegrant and dissolution agent used at 2–5% concentration in tablets prepared by direct-compression or wet- and dry-granulation methods. It rapidly exhibits high capillary activity and pronounced hydration capacity, with little tendency to form gels.

- Crospovidone can also be used as a solubility enhancer. With the technique of co-evaporation, crospovidone can be used to enhance the solubility of poorly soluble drugs.
- Studies suggest that the particle size of crospovidone strongly influences disintegration of analgesic tablets. Larger particle provides faster disintegration than smaller particles.
- Crospovidone can also be used as a solubility enhancer with the technique of coevaporation, crospovidone can be used to enhance the solubility of poorly soluble drugs. The drug is adsorbed on to crospovidone in the presence of a suitable solvent and the solvent is then evaporated. This technique results in faster dissolution rate.

Sodium Starch Glycolate

- **Non-proprietary Name**:
  - BP : Sodium Starch Glycollate
  - Ph Eur : Carboxymethylamylum natricum
  - USPNF : Sodium starch glycolate
- **Synonyms :**

Carboxymethyl starch, sodium salt; Explosol; Explotab; Glycolys; Primojel; starch carboxymethyl ether, sodium salt; Tablo; Vivastar P.

- **Chemical Name and CAS Registry Number:**
- Sodium carboxymethyl starch and [9063-38-1.]
- **Functional Category:**

Tablet and capsule disintegrant.

- **Applications in Pharmaceutical Formulation or Technology**

Sodium starch glycolate is widely used in oral pharmaceuticals as a disintegrant in capsule and tablet formulations.

- It is commonly used in tablets prepared by either direct compression or wet- granulation processes.
- Sodium starch glycolate has also been investigated for use as a suspending vehicle.

Sodium starch glycolate is widely used in oral pharmaceutical formulations and is generally regarded as a nontoxic and nonirritant material. However, oral ingestion of large quantities may be harmful.

Mannitol

Non-proprietary Name:

- BP : Mannitol
- JP : D-Mannitol
- PhEur : Mannitolum
- USP : Mannitol
- **Synonyms :**

Cordycepic acid; C*PharmMannidex; E421; manna sugar; D-mannite; mannite; Mannogem; Pearlitol.

- **Chemical Name and CAS Registry Number:**

D-Mannitol and [69-65-8.]

- **Empirical Formula and Molecular Weight**

$C_6H_{14}O_6$ and 182.17

- **Functional Category:**

Diluent; diluent for lyophilized preparations; sweetening agent; tablet and capsule diluent; tonicity agent.

- **Applications in Pharmaceutical Formulation or Technology**

- In pharmaceutical preparations it is primarily used as a diluent (10–90% w/w) in tablet formulations, where it is of particular value since it is not hygroscopic and may thus be used with moisture-sensitive active ingredients.
- Specific tablet applications include antacid preparations, glyceryl trinitrate tablets, and vitamin preparations.
- Mannitol is commonly used as an excipient in the manufacture of chewable tablet formulations because of its negative heat of solution, sweetness, and 'mouth feel'.
- Given orally, Mannitol is not absorbed significantly from the GI tract, but in large dosesit can cause osmotic diarrhea.

Aspartam

- **Non-proprietary Name**:
  - BP : Aspartame
  - PhEur : Aspartamum
  - USPNF : Aspartame
- **Synonyms :**

3-Amino-N-(a-carboxyphenethyl) succinamic acid N-methyl ester; 3-amino-N-(a-methoxy carbonylphenethyl) succinamic acid; APM; aspartyl phenylamine methyl ester; Canderel;E951; Equal; methyl N-a-L-aspartyl-L-phenylalaninate; NutraSweet; Pal Sweet; Pal Sweet Diet; Sanecta; SC-18862;Tri-Sweet.

- **Chemical Name and CAS Registry Number:**

N-a-L-Aspartyl-L-phenylalanine 1-methyl ester and [22839-47-0.]

- **Empirical Formula and Molecular Weight**

$C_{14}H_{18}N_2O_5$ and 294.31

- **Functional Category:**

Sweetening agent.

- **Applications in Pharmaceutical Formulation or Technology**

Aspartame is used as an intense sweetening agent in pharmaceutical preparations including tablets, powder mixes, and vitamin preparations. The approximate sweetening power is 180–200 times that of sucrose. Aspartame is metabolized in the body and consequently has some nutritive value. Therapeutically, aspartame has also been used in the treatment of sickle cell anemia.

Microcrystalline Cellulose (MCC)

- **Non-proprietary Name**:
  - BP : Microcrystalline cellulose.
  - PhEur : Cellulosum microcrystallinum.
  - USPNF : Microcrystalline cellulose.
- **Synonyms:**

Avicel PH, cellulose gel, emcocel, fibrocel,tabulose..

- **Chemical Name and CAS Registry Number:**

Cellulose. And [9004-34-6.].

- **Molecular Weight**:

36,000.

- **Structural Formula:**
- **Functional Category:**

Adsorbent, suspending agent, tablet and capsule diluent, tablet disintegrant.

- **Applications in Pharmaceutical Formulation or Technology:**

Microcrystalline cellulose is widely used in pharmaceuticals, primarily as a binder/diluent in oral tablet and capsule formulations where it is used in both wet granulation and direct compression processes. In addition to its use as a binder/diluent, microcrystalline cellulose also has some lubricant and disintegrant properties that make it useful in tableting.

Starch

- **Non-proprietary Names**
  - BP: Maize starch, Potato starch, Rice starch, Wheat starch,
  - JP: Corn starch,
  - PhEur: Maydis amylum (maize starch),
  - USPNF: Corn starch Tapioca
- **Synonyms**
  - Amido, amidon, amilo, amylum, Aytex P, C*PharmGel, Fluftex W, Instant Pure-Cote, Melojel, Meritena, Paygel 55.

❖ **Chemical Name and CAS Registry Number**
- Starch, [9005-25-8].

❖ **Empirical Formula and Molecular Weight**
- $(C_6H_{10}O_5)_n$ 50, 000–1, 60, 000.

Where n = 300–1000.

❖**Functional Category**
- Glidant; tablet and capsule diluents; tablet and capsule disintegrants; tablet binder.

❖ **Applications in Pharmaceutical Formulation or Technology**

❖Starch is used as an excipient, primarily in oral solid-dosage formulations where it is utilized as a binder, diluent, and disintegrant.

❖ As a diluent, starch is used for the preparation of standardized triturates of colorants or potent drugs to facilitate subsequent mixing or blending processes in manufacturing operations. Starch is also used in dry-filled capsule formulations for volume adjustment of the fill matrix.

❖ In tablet formulations, freshly prepared starch paste is used at a concentration of 5–25% w/w in tablet granulations as a binder. Selection of the quantity required in a given system is determined by optimization studies, using parameters such as granule friability, tablet friability, hardness, disintegration rate, and drug dissolution rate.

❖ Starch is one of the most commonly used tablet disintegrants at concentrations of 3–15% w/w. However, unmodified starch does not compress well and tends to increase tablet friability and capping if used in high concentrations. In granulated formulations, about half the total starch content is included in the granulation mixture and the balance as part of the final blend with the dried granulation. Also, when used as a disintegrant, starch exhibits type II isotherms and have a high specific surface for water sorption.

❖ Starch is also used in topical preparations, for example, it is widely used in dusting powders for its absorbency, and is used as a protective covering in ointment formulations applied to the skin. Starch mucilage has also been applied to the skin as an emollient, has formed the base of some enemas, and has been used in the treatment of iodine poisoning.

Magnesium Stearate

❖ **Non-proprietary Names:**
- BP: Magnesium Stearate
- JP: Magnesium Stearate
- PhEur: Magnesium Stearate
- USP-NF: Magnesium Stearate

❖ **Synonyms:**

Dibasic magnesium stearate; magnesium distearate; magnesia stearas; magnesium octadecanoate; octadecanoic acid, magnesium salt; stearic acid, magnesium salt; Synpro 90.

❖ **Chemical Name and CAS Registry Number:**
Octadecanoic acid magnesium salt [557-04-0]

❖ **Empirical Formula and Molecular Weight**:
$C_{36}H_{70}MgO_4$ and 591.24 g/mol

The USP/NF describes magnesium stearate as a compound of magnesium with a mixture of solid organic acids that consists chiefly of variable proportions of magnesium stearate and magnesium palmitate (C32H62MgO4).

The Ph.Eur. Describes magnesium stearate as a mixture of solid organic acids consisting mainly of variable proportions of magnesium stearate and magnesium palmitate obtained from sources of vegetable or animal origin.

❖ **Structural Formula**:
$[CH_3 (CH_2)16COO] 2Mg$

❖ **Functional Category**:
Tablet and capsule lubricant.

❖ **Applications in Pharmaceutical Formulation or Technology:**

Magnesium stearate is widely used in cosmetics, foods, and pharmaceutical formulations. It is primarily used as a lubricant in capsule and tablet manufacture at concentrations between 0.25% and 5.0% w/w. It is also used in barrier creams.

Talc

❖ **Non-proprietary Names:**
- BP : Purified talc
- JP : Talc
- PhEur : Talcum
- USP : Talc

❖ **Synonyms:**

Altalc; E553b; hydrous magnesium calcium silicate; hydrous magnesium silicate; Luzenac Pharma; magnesium hydrogen metasilicate; Magsil Osmanthus; Magsil Star; powdered talc; purified French chalk; Purtalc; soapstone; steatite; Superiore.

❖ **Chemical Name and CAS Registry Number:**
❖ Talc and [14807-96-6.]
❖ **Empirical Formula and Molecular Weight**:
❖ Talc is a purified, hydrated, magnesium silicate, approximating to the formula $Mg_6(Si2O5)_4(OH)_4$ and 379.3 g/mol
❖ **Functional Category**:
❖ Anticaking agent; glidant; tablet and capsule diluent; tablet and capsule lubricant

❖ **Applications in Pharmaceutical Formulation or Technology:**

Talc was once widely used in oral solid dosage formulations as a lubricant and diluent. In topical preparations, talc is used as a dusting powder, although it should not be used to dust surgical gloves. Talc is additionally used to clarify liquids and is also used in cosmetics and food products, mainly for its lubricant properties.

Equipment's Used

Sr. No	Equipment	Sr. No	Equipment
1	Tablet compression machine	11	LOD (Loss on drying) tester
2	Digital Balance	12	Hardness tester
3	Melting Point Apparatus	13	Density tester
4	Digital pH Meter	14	Blender
5	Rapid Mixer Granulator	15	Roche Friabilator USP
6	Planetary Mixer (PLM)	16	Vernier caliper
7	Disintegration tester	17	UV-Visible spectrophotometer
8	Dissolution apparatus		
9	Rapid Dryer		
10	FTIR Spectrophotometer -84005		

METHODS AND EVALUATION

PREFORMULATION STUDY

Preformulation testing was an investigation of physical and chemical properties of a drug substance alone and when combined with excipients. It was the first step in the rational development of dosage forms.

Active pharmaceutical ingredient (API) characterization:

Organoleptic evaluation: These are preliminary characteristics of any substance, which is useful in identification of specific material. Following physical properties of API were studied.

Loss on drying: 0.5g of sample of Active pharmaceutical ingredient was accurately weighed and the powder was kept in a Metter Toledo apparatus for 5 minutes at 105ºC and the moisture content was calculated (USP 39/NF 34, 2015).

Melting Point:

The determination of melting point during pre-formulation studies is important since it is a simple test gives valuable information regarding thermal properties of the material. Melting point was determined by capillary melting method (Electro lab Apparatus).

Solubility Profile

Solubility of API: The solubility was determined by weighing out 10mg of the compound (API) to this is added 10 micro-litre of the solvent interest, (such as water, DMF etc.). If not dissolved, further 40 micro-litre of solvent was added and its effect was noted. Successive amounts of the solvents were added until the compound was observed to dissolve.

pH Dependent Solubility Study of API:pH of Hydrocortisone in 10% solution (water) was found to be slightly acidic. The pH dependent solubility study was carried out by using different pH buffer solution ranging pH 1.2 (0.1 N HCl), pH 4.5 acetate buffer, pH 6.8 phosphate buffer and pH 8.4 phosphate buffer.

Drug– Excipients compatibility study: Drug–Excipients compatibility study of Active pharmaceutical ingredient with different categories of excipients was carried out. The compatibility of drug and formulation components is important prerequisite before formulation. It is therefore necessary to confirm that the drug does not react with the excipients under experimental conditions and affect the shelf life of product or any other unwanted effects on the formulation **(**as per ICH Q-1a, R2) guidelines).

Procedure: Active pharmaceutical ingredient is mixed with excipients in different ratio. These mixtures were kept in a 5ml glass white colored vials and packed with LDPE plug properly. These vials are exposed to 40°C/75%RH. 15gm of blend is prepared which is filled in 3 vials. Observations for physical appearance are made at initial, 2 week, and 4 week, the samples were withdrawn for analysis of following parameter.

The study was carried out according to ICH guidelines at different conditions of temperature and humidity like 40 ± 2ºC/ 75 ± 5% RH, room temperature by storing the samples i.e. Drug alone and along with the excipients in clear transparent glass vials stopper with LDPE plugs.

Selection of Super disintegrants: The best type of superdisintegrants are incorporated in the formulation of ODTs like,Sodium starch glycolate, Crospovidone, Cross carmellose sodium. Before the tablet formulation the superdisintegrants was screened out and taken into formulation with other excipients for compression by direct compression method. The superdisintegrant shows good properties like, when the tablet comes in contact with liquid, it breaks up into smaller particles because of superdisintegrants are swells, hydrate, change the volume and produce a disruptive change in the tablet.In this work, the direct compression method with aid of superdisintegrants was attempted for the formulation development of oral dispersible tablets of Active pharmaceutical ingredient. The superdisintegrants like Sodium starch glycolate, Crospovidone, Cross carmellose sodium were taken for the formulation development.

Preparation of powder blend of drug and excipients:

The powder blend for oral dispersible tablets were prepared by taking ingredients given in All the ingredients were passed through 60 mesh sieve separately and collected. Then ingredients were weighed and mixed in a geometrical order.

Pre-compression assessment of powder blend

Different parameters were evaluated for prepared powder blend using following methods.

Angle of repose Angle of repose has been used to characterize the flow properties of solids. This is the maximum angle possible between surface of pile of powder or granules and the horizontal plane.

$$\tan \theta = h / r$$
$$\theta = \tan^{-1}(h / r)$$

Where, θ = angle of repose, **h** = height of heap, & **r** = radius of base of heap circle.

A funnel was fixed at a height approximately 2-4 cm over the platform. The loose powder was slowly passed along the wall of funnel, till the tip of powder cone so formed just touched the tip of funnel stem. Angle of repose was then determined by

Measuring the height of the cone of powder and radius of the circular base of powder heap (USP 39/NF 34(2015)).

Angle of repose of powder less than 30^0 are usually indication of good flow, powder with angles greater than 40^0 are likely to be problematic

Flow Properties and Corresponding Angle of Repose

Sl. No.	Flow property	Angle of repose (^{0})
1.	Excellent	25-30
2.	Good	31-35
3.	Fair – aid not needed	36-40
4.	Passable - may hang-up	41-45
5.	Poor – must agitate, vibrate	46-55
6.	Very poor	56-65
8.	Very, very poor	>66

Compressibility Index Compressibility index has been proposed as an indirect measure of bulk density, size and shape, surface area, moisture content, and cohesiveness of materials because all of these can influence the observed compressibility index. The compressibility index and Hausners ratio are determined by measuring both bulk density and the tapped density of a powder.

$$\text{Compressibility Index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

The density analysis was carried out by using USP Type-1 apparatus.

Hausner Ratio:

Hausner ratio was determined by measuring both bulk density and the tapped density of a powder (USP 39/NF 34(2016)).

$$\text{Hausner Ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

The Hausner Ratio varies from about 1.2 for free flowing powder to 1.6 for cohesive powders.

Relation between Compressibility Index and Hausner Ratio

S No.	Compressibility Index (%)	Flow Character	Hausner Ratio
1.	≤ 10	Excellent	1.00 – 1.11
2.	11 – 15	Good	1.12 – 1.18
3.	16 – 20	Fair	1.19 – 1.25
4.	21 – 25	Passable	1.26 – 1.34
5.	26 – 31	Poor	1.35 – 1.45
6.	32 – 37	Very poor	1.46 – 1.59
8.	> 38	Very, very poor	> 1.60

Post-compression assessment of powder blend

Hardness = Hardness of the tablet was determined by using Monsanto tablet hardness tester. Hardness or tablet crushing strength (fc), the force required to break a tablet in a diametric compression. From each batch, hardness of 6 tablets was determined. The lower plunger is placed in contact with tablet, and a zero reading was taken. The upper plunger is then forced against a spring by turning a threaded bolt until the tablet fractures. Hardness of tablet is expressed in kg / cm2.

Friability= The friability test for tablets was performed to assess the effect of abrasion and shocks. Roche Friabilator was used for the percent friability of the tablets. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at a height of 6 inches in each revolution. Pre-weighted sample of tablets was placed in the Friabilator and were subjected to the

100 revolutions. Then the tablets were removed and de dusted by using a soft muslin cloth and reweighed. The weight lost should not exceed the limit 1.0%. The percentage friability was measured by using the following formula.

$$\% F = \frac{W_{initial} - W_{Final}}{W_{initial}} \times 100$$

Where
% F = Friability in percentage,
W initial = Initial weight of tablet
W final = Final weight of tablet.

Thickness The thickness of tablets was measured by using Vernier caliper. Five tablets from each batch were taken randomly and thickness was measured and average values were calculated. Thickness is expressed in mm.

Weight Variation The weight variation test was performed as per I.P. twenty tablets were randomly selected from each batch and individually weighed. And then average weight was calculated from the total weight of all tablets. The individual weights were compared with the average weight. The tablets passes the test for weight variation test if no more than two tablets are outside the percentage limit and if no tablet differs by more than two times the percentage limit. Weight variation specification as per I.P. is shown in Weight variation tolerances for uncoated tablets

Average weight of tablets (mg)	% Deviation
80 mg or less	±10
More than 80 mg and less than 250mg	±8.5
250 mg or more	±5

***In-vitro* Dispersion Time**
In-vitro dispersion time was measured by dropping a tablet into a petridish containing 10ml of phosphate buffer pH 6.8 solution at 37± 0.50c. Three tablets from each batch were randomly selected and tested the time required for complete dispersion of a tablet was measured. The *in-vitro* dispersion time is expressed in seconds.

Wetting Time A piece of tissue paper folded double was placed in a Petri dish (6.5cm) containing 6 ml of water .the tablet was placed on the paper, and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 370c.Wetting time corresponding to the time taken for the tablet to disintegrate when kept motionless on the Petri dish.

Water Absorption Ratio A piece of tissue paper folded twice was placed in a petri dish (6.5cm) containing 6 ml of water. A tablet was put on the tissue paper and the time required for the complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R, was determined using following equation.

$$\% F = \frac{(Wa - Wb)}{Wb} \times 100$$

Where, Wa = Weight of the tablet after absorption, Wb = Weight of the tablet before absorption.

Disintegration Time:It is determined by using USP device which consist of 6 glass tubes that are 3 inches long, open at one end and held against 10 mesh screen at the bottom end of basket rack assembly. To test for disintegration time, one tablet is placed in each tube and the basket arch is positioned in a1 liter beaker of water at 37˚C ± 2˚C.A standard motor driven device is used to move the basket assembly up and down (USP39/NF34). To be incompliance with the USP standard, all tablets must disintegrate and all particles must pass through the 10 mesh in the time specified.

Content uniformity:
The drug content of the tablets was measured UV spectrophotometry, in USP It has been reported that Hydrocortisone can be detected at 245 & 248 nm. Each tablets containing 20mg of Hydrocortisone was placed in 100ml volumetric flask to it 70 0.1N HC is added and sonicated until to complete extraction and then equilibrated at room temperature then volume make up to the mark. Moreover diluted taking 5 ml from stock solution to dissolve in 50ml volumetric flask. (Concentration = 20ppm solution). Drug content uniformity was carried out at 245 nm with comparing standard prepared solution.

In –vitro Dissolution Test:

a) Standard solution Preparation
Take 22 mg of Active pharmaceutical ingredient working standard into a 100ml volumetric flask, dissolve and makeup to the volume with diluents. Dilute 5 ml of the above solution to 50ml with diluent. (Concentration = 20 ppm solution)

b) Sample solution Preparation
Dissolution study of tablet performed in USP II (paddle) dissolution test apparatus (Electro lab TDL O8L) using 900 ml of water as a dissolution media. The tablet was placed in to the vessel of dissolution apparatus; the temperature of dissolution media was maintained

at 37°C ± 5°C. With stirring speed of 50 rpm throughout the study. Aliquots of dissolution media containing 10ml of samples were withdrawn at time interval of 1, 2, 3, 4 and 5 minutes and 10ml of fresh dissolution media maintained at the same temperature was replaced after each withdrawal. The raw dissolution data was analyzed for calculating the amount of drug released and percentage cumulative drug released by recording absorbance at 248nm wavelength. (Concentration = 22 ppm solution)

Dissolution Parameters

Drug Name	Dosage Form	USP Apparatus	Speed (RPMs)	Medium	Volume (ml)	Sampling Time Points (minutes)
Active pharmaceutical ingredient	Tablet	II (Paddle)	50	0.1 N HCL	900	1, 2, 3, 4,5,6 and 7

Calculations:

$$\% \text{ of Drug dissolved} = \frac{A_T \times W_{std} \times 5 \times 900 \times 100 \times 1}{A_S \times 100 \times \text{Sample} \, L.C \times 20}$$

Where,

A_T = Average of the absorbance count of the Hydrocortisone test aliquots.

A_S = Average of the absorbance count of the Hydrocortisone standard.

W_{std} = Weight of the working standard taken in mg.

L.C. = Label claim in mg.

P = % potency of Hydrocortisone l working standard.

Stability Studies

1) Short -term stability studies

2) **Long - term stability studies**

Table 8.6. Stability conditions according to ICH guidelines

Types	Conditions		Minimum time period at submission (month)
	Temperature (0 C)	Relative humidity (%)	
Short-term testing	40 ± 2	75 ± 5	6
Long-term testing	25 ± 2	60 ± 5	12

Method:

Selected formulations were stored at different storage conditions at elevated temperatures such as 25oC± 2^0C / 60% ± 5% RH, and 400C ± 2^0C/ 75% ± 5% RH for 90 days. The samples were withdrawn at intervals of 30 days and checked for physical changes, hardness, friability, drug content and percentage drug release.

REFERNCES

1. Venkatesh, Gopi M., Phillip J. Stevens, and Jin-Wang Lai. "Development of orally disintegrating tablets comprising controlled-release multiparticulate beads." *Drug development and industrial pharmacy* 38, no. 12 (2012): 1428-1440.
2. Wang, Ling, Fan Zeng, and Li Zong. "Development of orally disintegrating tablets of Perphenazine/hydroxypropyl-β-cyclodextrin inclusion complex." *Pharmaceutical development and technology* 18, no. 5 (2013): 1101-1110.
3. Ghosh, Tanmoy, Amitava Ghosh, and Devi Prasad. "A review on new generation orodispersible tablets and its future prospective." *International journal of pharmacy and pharmaceutical sciences* 3, no. 1 (2011): 1-7.
4. Bandari, Suresh, Rajendar Kumar Mittapalli, and Ramesh Gannu. "Orodispersible tablets: An overview." *Asian Journal of Pharmaceutics (AJP): Free full text articles from Asian J Pharm* 2, no. 1 (2014).
5. Wagh, Manoj Ashok, Dilip Parag Kothawade, Kishor Sahebrao Salunkhe, Nayana Vijay Chavan, and Vandana Radheshyam Daga. "Techniques used in orally disintegrating drug delivery system." *International journal of drug delivery* 2, no. 2 (2010).
6. Petkar, Kailash C., Sandip S. Chavhan, Snezana Agatonovik-Kustrin, and Krutika K. Sawant. "Critical Reviews™ in Therapeutic Drug Carrier Systems."
7. Gupta, A., A. K. Mishra, V. Gupta, P. Bansal, R. Singh, and A. K. Singh. "Recent trends of fast dissolving tablet-an overview of formulation technology." *International Journal of Pharmaceutical & Biological Archives* 1, no. 1 (2010): 1-10.
8. Shukla, Dali, Subhashis Chakraborty, Sanjay Singh, and Brahmeshwar Mishra. "Mouth dissolving tablets I: An overview of formulation technology." *Scientia Pharmaceutica* 77, no. 2 (2009): 309-326.
9. Suresh, Sarasija, and H. P. Joshi. "Preparation and evaluation of mouth dissolving tablets of salbutamol sulphate." *Indian journal of pharmaceutical sciences* 69, no. 3 (2007): 467.
10. Kumar, Erande, and Joshi Bhagyashree. "Mouth dissolving tablets–A comprehensive review." *International Journal of Pharma Research & Review* 2, no. 7 (2013): 25-41.
11. Pahwa, Rakesh, Mona Piplani, Prabodh C. Sharma, Dhirender Kaushik, and Sanju Nanda. "Orally disintegrating tablets-Friendly to pediatrics and geriatrics." *Archives of applied science research* 2, no. 2 (2010): 35-48.

12. Hirani, Jaysukh J., Dhaval A. Rathod, and Kantilal R. Vadalia. "Orally disintegrating tablets: a review." *Tropical journal of pharmaceutical research* 8, no. 2 (2009).
13. Ganesh, N. S., and K. B. Deshpande. "Orodispersible tablets: an overview of formulation and technology." *International Journal of Pharma and Bio Sciences* 2, no. 1 (2011): 726-734.
14. Gohel, Mukesh, Madhabhai Patel, Avani Amin, Ruchi Agrawal, Rikita Dave, and Nehal Bariya. "Formulation design and optimization of mouth dissolve tablets of nimesulide using vacuum drying technique." *AAPs PharmSciTech* 5, no. 3 (2004): 10-15.
15. Craig, Duncan QM, Paul G. Royall, Vicky L. Kett, and Michelle L. Hopton. "The relevance of the amorphous state to pharmaceutical dosage forms: glassy drugs and freeze dried systems." International journal of pharmaceutics 179, no. 2 (1999): 179-207.