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Review On Excipients Used In Immediate release Tablets Formulation

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Abstract:

Immediate release tablets are widely employed in pharmaceutical formulations to achieve rapid drug delivery. The success of these formulations heavily relies on the careful selection and optimization of excipients. This review aims to provide an in-depth analysis of the excipients commonly used in immediate release tablet formulations, their functions, selection criteria, and their impact on drug release profiles. Understanding the role of excipients in immediate release tablet formulations is crucial for formulators to develop effective and efficient dosage forms.

Keywords: Immediate release, approaches, excipients, polymer,incompatibilities.

1.Introduction

Immediate release tablets are a commonly used oral dosage form in the pharmaceutical industry.They are designed to deliver the active ingredient quickly and efficiently into the systemic circulation upon ingestion. Immediate release tablets are formulated to disintegrate rapidly and release the drug for prompt absorption, resulting in a rapid onset of therapeutic action. They are particularly suitable for drugs that require immediate or fast absorption, such as pain relievers, antacids, and anti-infectives.

The main objective of immediate release tablets is to provide a rapid and predictable release of the drug, allowing for optimal therapeutic outcomes. They offer several advantages over other dosage forms, including convenience, ease of administration, accurate dosing, and flexibility in formulation design. Immediate release tablets are available in a wide range of strengths, sizes, and shapes to accommodate different patient populations and dosage requirements.

The formulation of immediate release tablets involves a careful selection of excipients and optimization of their proportions to achieve desired tablet characteristics and drug release profiles. Excipients are inactive substances that play crucial roles in tablet formulation, including enhancing tablet compressibility, ensuring uniform drug

distribution, promoting tablet disintegration, and improving stability. Diluents, binders, disintegrants, lubricants, glidants, and coating agents are some of the key excipients used in immediate release tablet formulations.

In addition to the selection of excipients, other factors such as drug solubility, permeability, and stability must be considered during the formulation process. The physicochemical properties of the active ingredient, such as particle size, crystal form, and hydrophobicity, can influence the choice of excipients and formulation strategies.

Regulatory bodies, such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), provide guidelines and specifications for the development and evaluation of immediate release tablets. These guidelines ensure that the tablets meet quality, safety, and efficacy standards, including appropriate dissolution profiles and content uniformity.

1.1 Basic Physiology of immediate release tablets

The basic physiology of immediate release tablets involves several key processes that occur in the body after ingestion.Here is a simplified overview of all the physiological events associated with immediate release tablets:

Oral Administration: The immediate release tablet is taken orally with water or another suitable liquid. The tablet is swallowed and enters the gastrointestinal tract.

Disintegration: Once the tablet reaches the stomach, it begins to disintegrate rapidly due to the presence of disintegrants in the formulation. Disintegrants promote the breakup of the tablet into smaller particles, increasing the surface area available for drug dissolution.

Drug Dissolution: As the tablet disintegrates, the drug particles are exposed to the gastric fluid. The drug molecules dissolve in the fluid, forming a solution or suspension. The dissolution process is influenced by factors such as drug solubility, particle size, and formulation characteristics.

Absorption: After dissolution, the drug molecules move from the gastrointestinal tract into the bloodstream through various mechanisms. Most absorption of drugs from immediate release tablets occurs in the small intestine, where the large surface area of the intestinal lining facilitates efficient absorption. The drug molecules cross the intestinal epithelium and enter the portal circulation, reaching the liver.

Distribution and Systemic Effects: Once in the bloodstream, the drug molecules are transported throughout the body, reaching the target tissues or organs. The drug exerts its pharmacological effects by interacting with specific receptors or biological targets. The onset of action is relatively rapid for immediate release tablets due to the prompt absorption of the drug.

Metabolism and Elimination: In the liver, the drug may undergo various metabolic processes, such as biotransformation, to form metabolites. Metabolism can alter the drug's activity, potency, and duration of action. The drug and its metabolites are eventually eliminated from the body through processes such as renal excretion, hepatic excretion, or metabolism into inactive compounds.

1.2 Advantages and Disadvantages of Immediate release tablets

1.2.1 Advantages of immediate release tablet

- Rapid Onset of action
- Convenience and ease of administration
- Accurate dosing
- Immediate drug delivery of dosage form
- Flexibility in formulation design

- Cost effectiveness

1.2.2 Disadvantages of Immediate release tablets

- Short duration of action
- Potential for fluctuating blood concentrations
- Require more frequent dosing
- Gastrointestinal irritation
- Limited control over drug release

1.3 Potential Drug Aspirants for immediate release tablets

There are numerous drugs that are suitable for immediate release tablets.The selection of a drug for immediate release tablet formulation depends on various factors, including its therapeutic indication, pharmacokinetic properties, and patient requirements. Here are some examples of drugs commonly formulated as immediate release tablets:

1. Analgesics and Anti-inflammatory Drugs:

   Acetaminophen (Paracetamol)

   Ibuprofen

   Naproxen

   Diclofenac

- Antipyretics:

  Aspirin

  Acetaminophen (Paracetamol)

- Antihistamines:

  Diphenhydramine

  Loratadine

  Cetirizine

- Antacids and Acid Reducers:

  Calcium carbonate

Ranitidine

Famotidine

Omeprazole

- Anti-infectives:

  Amoxicillin

  Cephalexin

  Azithromycin

  Metronidazole

- Cardiovascular Drugs:

  Metoprolol

  Amlodipine

  Lisinopril

  Nitroglycerin

- Respiratory Medications:

  Albuterol

  Montelukast

  Ipratropium

  Theophylline

- Gastrointestinal Drugs:

  Ondansetron

  Loperamide

  Mebeverine

  Domperidone

- Anti-diabetic Medications:

  Metformin

  Gliclazide

  Glipizide

- Sedatives and Hypnotics:

  Diazepam

  Zolpidem

  Lorazepam

1.4 Approaches for Immediate release tablets

There are several approaches for immediate release tablets .Some of them are discussed below:

Direct Compression: This approach involves directly compressing a mixture of API and excipients without prior granulation .It is a simple and cost-effective method, particularly suitable for drugs with good flow and compressibility properties.It requires carefully selected excipients to ensure proper flow, uniformity, and tablet hardness.

Wet Granulation:Wet granulation involves the formation of granules by adding a liquid binder to a mixture of API and excipients, followed by drying and milling before compression. This method improves flowability , compressibility, and uniform drug distribution. It is Commonly used for drugs with poor flow and compression characteristics or when modified release formulations are desired.

Dry Granulation:Dry granulation also known as slugging or roller compaction, involves compacting the API and excipient mixture into large tablets or slugs,followed by milling and sizing , and then compressing into final tablets.This approach is suitable for moisture sensitive drugs or those with poor compressibility.It eliminates the need for a liquid binder reducing potential stability issues.

When selecting an approach for immediate release tablets, factors such as the physicochemical properties of the drug, target release profile, manufacturing capabilities, stability, and patient acceptability should be considered. Each approach has its own advantages and challenges, and the formulation scientist must choose the most appropriate approach based on the specific requirements of the drug product.

1. **Excipients**

An excipient is a pharmacologically inactive component formulated with the active pharmaceutical ingredient of a dosage form. Excipients serve the following purposes:

• They give the formulation bulk.
• Facilitate drug solubility or absorption, as well as other pharmacokinetic factors.
• Assist with handling "API" during production.

• Offer stability and guard against denaturation, etc.

The characteristics of excipients are no medication interactions, inert pharmacologically, feasible. Example of excipients are Fillers, Binders, Disintegrants, Coating, Sorbents. Antiadherent. Lubricants. Glidants. Preservatives. Antioxidants. Aromatic agents. Sweeting Agents. Agents for coloring. Co-solvent and Solvent Agents for buffering. Cheating Tools. Agents that impart viscosity. Agents with Surface Activity. humectant. Mechanism & interference of the excipient determination of whether or not a drug succeeds or fails. If the best excipient is not selected for a formulation, it may result in manufacturing issues, impaired stability,inadequate API bioavailability, unanticipated side effects, potentially major adverse reactions or patient mortality. Therefore, it is crucial to choose the correct excipient for the formulation and ensure its quality in order to avoid these undesired effects.[1]

Polymers have long been employed in medication delivery systems as pharmaceutical excipients.
Increased solubility, swellability, viscosity, biodegradability, advanced coatings, pH dependencemucodhesion, and crystallization inhibition.[9,10]
Polymers: Derive from the Greek word (*polus*, meaning "many, much") and (*meros*, meaning "part"), and Polymers are big molecules with a structure made up of several repeating units, from which they get their high relative molecular mass and other attributes. The units that make up polymers come from molecules with a low relative molecular mass, either physically or conceptually.[10,11]

2.1 Types of polymer used in Immediate release tablets

- Cellulose Derivatives:

  Hydroxypropyl cellulose (HPC)

  Hydroxypropyl methylcellulose (HPMC)

  Methylcellulose (MC)

  Ethylcellulose (EC)

- Polyvinyl Pyrrolidone (PVP):

  PVP K-30

  PVP K-90

  PVP K-120

- Acrylic Polymers:

  Poly(methacrylic acid-co-ethyl acrylate) (PMA/EA)

  Eudragit® RS (poly(methacrylic acid-co-methyl methacrylate))

  Eudragit® RL (poly(methacrylic acid-co-methyl methacrylate))

- Polyethylene Oxide (PEO):

  Polyethylene glycol (PEG)

  Polyethylene oxide (PEO)

- Polyvinyl Alcohol (PVA)

- Polyethylene Glycol (PEG)

- Polymeric Excipients:

  Sodium carboxymethyl cellulose (CMC)

  Croscarmellose sodium

  Sodium starch glycolate

  Crospovidone

- Copovidone (polyvinyl acetate/polyvinylpyrrolidone copolymer)
- Starch and its Derivatives:

  Starch

  Modified starches

- Poloxamers (Pluronics)

These polymers are selected based on their properties such as solubility, swelling behavior, viscosity, film-forming capability, and compatibility with the drug and other excipients. They can be used alone or in combination to achieve the desired drug release profile and tablet characteristics. The selection of a specific polymer depends on factors such as the drug's physicochemical properties, required release kinetics, target site of action, and manufacturing considerations.

2.2 Ideal properties of Excipients:

1. Feasible
2. Pharmacologically inert
3. Stable for handling
4. Cost Effective
5. No interaction with drug
6. Conistency for drug release
7. Patient Compliance

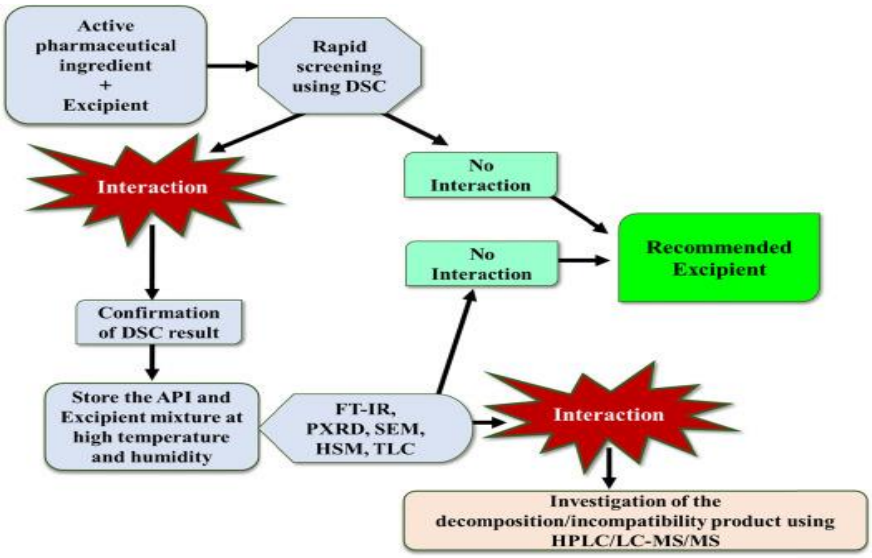

Fig 1: Selection Of Excipient Criteria

2.3 Mechanism of drug-excipient intractions

They can be classified as-

1. Physical interaction
2. Chemical interaction
3. Biopharmaceutical interaction
4. Excipient –Excipient interactions[12,13,14,15]

1. Physical interaction

Change dose consistency,color,flavor,solubility,stability, or sedimentation rate among other things.These interactions might have a positive or negative impact on the products performance.

2. Chemical Interactions

It entails a chemical reaction between medications and excipients , or between drugs and impurities/residues in excipients, to produce distinct molecules. Chemical interaction yield degradation products which are virtually always damaging to the product.

3. Biopharmaceutical interactions

These are the interactions that occurred after the drug was administered.Medicine and bodily fluids interact within the body ,affecting the rate of absorption. When taken with active medicinal components ,all excipients have a physiological effect.

Enteric coating polymers such as cellulose acetate and hydoxy propyl cellulose acetate phthalate are examples of enteric coating polymers that break down prematurely.Are more soluble at a basic PH, but antacids elevate the PH of the stomach, Causing the enteric coat to break down and the active pharmaceutical ingredient to be released in to the stomach,resulting in drug degredation in the stomach. Premature breakdown of the enteric coat caused by NSAIDS might result in side effects such as gastrointestinal hemorrhage.

4. Excipient-excipent interaction

Excipient-excipient interaction is a rare occurance. These factors are crucial in determining the doses forms stability. Interactions between excipients might be undesired, however some interactions are exploited in formulations to achieve the desired product qualities.

The most common excipients used for immediate release tablets are as follows:

S.No	Excipient	Function	Examples
1	Fillers/Diluent	Provide bulk and enable accurate dosing of potent ingredients	• Lactose • Microcrystalline cellulose (MCC) • Dicalcium phosphate • Mannitol • Starch
2	Binders,compression aids,granulating agnets	Bind the tablet ingredients together giving form and mechanical strength, release drug in sustained manner	• Hydroxypropyl cellulose (HPC) • Hydroxypropyl methylcellulose (HPMC) • Polyvinylpyrrolidone (PVP) • Sodium carboxymethyl cellulose (CMC)
3	Disintegrants	Aid dispersion of the tablet in the gastrointestinal tract,releasing the active ingredient and increasing the surface area for dissolution	• Croscarmellose sodium • Sodium starch glycolate • Crospovidone • Cross-linked PVP
4	Glidants	Improve the flow of	• Colloidal silicon

		powders during tablet manufacturibg by reducing friction adhesion between particles. Also used as Anticaking agent	dioxide (Aerosil) • Talc • Starch
5	Lubricants	Similar action to glidants,however,they may slow disintegration and dissolution. The properties of glidants and lubricants differ, although some compinds, such as starch and talc have both actions	Stearic acid and its salts(e.g magnesium stearate,calcium stearate
6	Tablet Coatings and films	Protect tablet from the environment(air,light and moisture), increase the mechanical strength , mask tate and smell,aid swallowing,assist in product identification. Can be used to modify release of the active ingredient. May contain flavours and colourings	• Hydroxypropyl methylcellulose phthalate (HPMCP) • Hydroxypropyl methylcellulose acetate succinate (HPMCAS) • Polyvinyl alcohol (PVA) • Shellac

Table 1:Excipients used in immediate release tablets

2.4 Experimental design of compatibility Study

1. Two or Multi-Component Systems
   Binary mixture of drug and pharmaceutical excipients such as diluents & disintegrates and lubricants which are used as lower proportions . These are incubated at accelerated conditions of temperature and humidity for extended periods of time using drug alone & excipients alone as controls.
2. n-1 Design & Mini formulation
   Compatibility studies are often aimed at solving formulation stability issues. In such cases studies are carried out with the exclusion of only one component in each sub-lot to identify the source of incompatibility. Often, mini-formulations are prepared with the exclusion of non-critical, quantitatively minor, and/or easily interchangeable ingredients, e.g., colors and flavors, from solutions and suspensions.

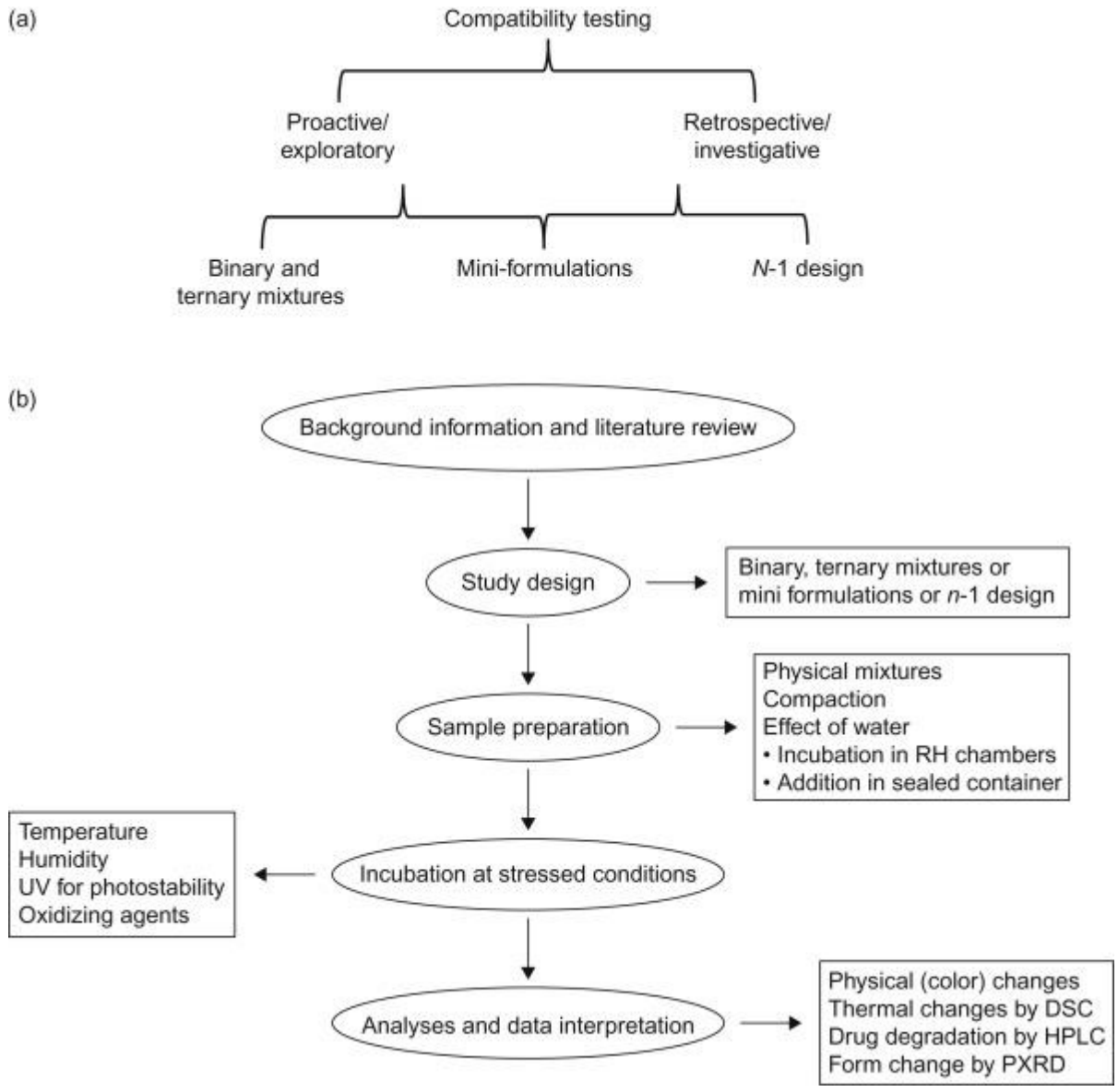

Fig 2: Step in Compatibility study

3.Steps in compatibility study

There are THREE steps to consider

1. Sample preparation

2. Storage
3. Method of analysis

3.1 Sample preparation

For solid state reactions:
Sample A: -mixture of drug and excipient
Sample B: -Sample A+ 5% moisture
Sample C: -Drug itself without excipients
All the samples of drug-excipient blends are kept for 1-3 weeks at specified storage conditions. Then sample is physically observed . It is then assayed by TLC or HPLC or DSC. Whenever feasible, the degradation product are identified by MASS SPECTROSCOPY, NMR or other relevant analytical techniques. To determine Solid state stability profile of a new compound. To test the Surface Oxidation.

For liquid state reactions:
Place the drug in the solution of additives. Both flint and amber vials are used. This will provide information about -Susceptibility to oxidation. -Susceptibility to light exposure. -Susceptibility to heavy metals. In case of oral liquids, compatibility with ethanol, glycerin , sucrose, preservatives and buffers are usually carried out.

3.2 Storage conditions. The storage conditions used to examine compatibility can very widely in term of temp & humidity, but a temp of 50°c for storage of compatibility sample is considered appropriate. Some compounds may require high temp.to make reaction proceed at a rate that can be measured over a convenient time period.

4. ANALYTICAL TECHNIQUES USED TO DETECT DRUGS-EXCIPIENTCOMPATIBILITY

1. Thermal methods of analysis – DSC- Differential Scanning Calorimetry – DTA- Differential Thermal Analysis
2. Accelerated Stability Study
3. FT-IR Spectroscopy
4. DRS-Diffuse Reflectance Spectroscopy
5. Chromatography – SIC-Self Interactive Chromatography – TLC-Thin Layer Chromatography – HPLC-High Pressure Liquid Chromatography
6. Miscellaneous – Radiolabelled Techniques – Vapour Pressure Osmometry – 7.Flourescence Spectroscopy
8.DSC- DIFFERENTIAL SCANNING CALORIMETRY

DSC is widely used to investigate and predict any physico-chemical interaction between drug and excipients involving thermal changes.

METHOD -The preformulation screening of drug-excipient interaction requires
(1:1) Drug:excipient ratio, to maximize the likehood of observing an interaction. Mixture should be examined under N2 to eliminate oxidative and pyrrolytic effects at heating rate (2,5 or 100 c / min) on DSC apparatus. [18,19,20]

Sumarized of Instrument in Drug-Excipient Compatibility Study

Sr. no.	Investigative technique	Measurement	Utility of data
1	DSC	Energy is absorbed or released by a sample as it is heated, cooled, or held at a constant Temperature	Physicochemical compatibility of drug and Excipients
2	TGA	Weight changes by a sample as it is heated, cooled, or held at a constant temperature	Physicochemical compatibility of drug and Excipients
3	Chromatographic analysis	Chemical interactions of the sample with the stationary phase and the mobile phase	Excipients, drug product purity; excipient–drug substance chemical compatibility
4	Microcalorimetry	Absorbance or release of heat from solution sample	Physicochemical compatibility of drug and excipients; solution applications
5	X-ray diffraction	Scattering of x-ray radiation by a solid sample	Polymorph characterization
6	Microscopy	Magnified appearance of sampl	Particle size, morphology
7	LC-MS/MS	Chromatographic separation and fragmentation of molecular species	Impurity, degradation product identification

Table 6: Sumarized of Instrument in Drug-Excipient Compatibility Study

Future Potential

Improved drug delivery technologies: Advancements in drug delivery technologies may lead to more efficient and targeted release of medications. Nanotechnology, microencapsulation, and other innovative delivery systems could enhance the bioavailability and stability of drugs in immediate-release tablets.

Personalized medicine: The future of pharmaceuticals might see the rise of personalized medicine, where immediate-release tablets are tailored to individual patients based on genetic factors, metabolism rates, and specific health needs. This could optimize treatment effectiveness and minimize adverse effects.

Combination therapies: Immediate-release tablets could be used to deliver multiple drugs simultaneously or in a staggered manner to treat complex medical conditions more effectively. This approach might lead to better patient compliance and outcomes.

Biodegradable and eco-friendly formulations: With a growing focus on sustainability and environmental impact, there might be a push towards developing biodegradable materials for tablet coatings and packaging, reducing waste and environmental footprint.

Smart pills and digital health integration: Future immediate-release tablets could be equipped with embedded sensors or tracking technologies to monitor drug adherence and physiological responses. These smart pills could integrate with digital health platforms to provide real-time health data to patients and healthcare providers.

Continuous release systems: The development of novel continuous release systems could further extend the duration of drug action, enabling less frequent dosing and better management of chronic conditions.

Combination of drugs and natural compounds: Combining traditional pharmaceuticals with natural compounds or extracts might become more prevalent in immediate-release tablets, potentially leading to enhanced therapeutic effects and reduced side effects.

Regulatory advancements: Regulatory agencies may develop new guidelines or expedited approval processes for immediate-release tablets that demonstrate superior safety, efficacy, or patient benefits.

Conclusion:

Excipients are skeletal for dosage form which gives shape ,size & complete finishing to dosage forms. Each and every excipients are not suitable for Active Pharmaceutical Ingredient. Drug-Excipients Comptability study should be done before choosing excipients over the formulation. However different types of immediate release dosage form are available choosing of excipients is directly proportional to its method. Polymer selection seems more challenging because of many types of polymer like natural,semisynthetic & synthetic .

References

1.Lachman/Lieberman's ,The theory and practice of Industial Pharmacy: Fourth edition

2.Mishra B, Rajinikanth PS. Floating in situ gelling system for stomach site- specific delivery of clarithromycin to eradicate H. pylori. Journal of Controlled Release 2008.

3.Biradar SS, Bhagavati ST, Kuppasad IJ. Fast dissolving drug delivery systems: A brief overview. International Journal of Pharmaceutical Sciences, 2006; 4(2).

4.Wael Ali, Alia A. Badawi, Mahmoud A. Mahdy, Hanan M. ElNahas, Formulation and evaluation of carbamazepine 200mg immediate release tablets using polyethylene glycol 6000, Int J Pharm Pharm Sci, 2013, 5 (l):114-119.

5.Niranjan Panda, Afshan Sultana, A Venkateswar Reddy, G. V. Subba Reddy, M.S.Ansari: Formulation Design and Study the effect of Polyplasdone-XL and AC-Di-Sol on Release Profile of Doxofylline Immediate Release Tablets. Int. J. Pharm. Sci. Rev. Res., 32(2), 2015: 67-76.

6.Prajapati ST, Patel MV, Patel CN; 2014. Preparation and evaluation of sublingual tablets of Zolmitriptan. International Journal of Pharmaceutical Investigation. 4, 27-31.

7.Akbar, N. Panda, AV Reddy, "Formulation and Evaluation of Doxofylline Sublingual Tablets Using Sodium Starch Glycolate and Crosscarmellose Sodium as Superdisintegrant" Int. J. of Pharm. Res. & All. Sci. 2015; 4(2):90-100

8.Sudhir. Maddela, Eswar Gupta. Maddi and Ramarao. Nadendla, Immediate Release Formulation of Valsartan Capsule and Evaluation of its Compatibility by Nonthermal Methods, American Journal of Advanced Drug Delivery, 1 (3), 2013, 180-196.

9. Patel DM, Patel SP, Patel CN. Formulation and evaluation of fast dissolving tablet containing Domperidone ternary solid dispersion. Int J Pharma Investig 2014;4:174-82.

10. Shailesh T Prajapati, Parth B Patel, Chhagan N Patel, Formulation and evaluation of sublingual tablets containing Sumatriptan succinate, Int Jour of Pharma Invest, 2012, 2(3), 162-168. Md Sarfaraz, V.G.Joshi, Immediate release solid oral dosage form of salbutamol sulphate:design, optimization and evaluation, Int J Pharm Pharm Sci, 2013, 5 (4): 610-618.

11.Kumar VD, Sharma I., Sharma V. A comprehensive review on fast dissolving tablet Technology, Journal of Applied Pharmaceutical Science, 2011, 01 (05):50-58.

12.Siddiqui MN, Garg G., Sharma PK. Fast Dissolving Tablets: Preparation, Characterization and Evaluation: An Overview, International Journal of Current Pharmaceutical Research, 2008, 15(4).

13. Roden DM, Antiarrhythmic Drugs, In: Goodman and Gilman's Pharmacology Basis of Therapeutics, 10th ed., McGraw Hill Publishing Division, New York 2006, 949-50.

14.Koteswari P, Sunium S, Srinivasababu P, Babu GK, Nithya PD. Formulation Development and evaluation of fast disintegrating tablets of Lamotrigine using liqui-solid technique. Int J Pharma Investig 2014;4:207-14.

15. Naik PS., Kurup NS. Design and optimization of fast dissolving tablets containing metoprolol by sublimation method. IRJP.2010;1(1): 346-357.

16. Palkhede M., Amrutkar S., Erande K.. Formulation, optimization and evaluation of fast disintegrating tablet of mebeverine HCl. Int J Pharm Pharm Sci. 2012; 4(4):121-125.

17.Agarwal, P. V. K Kumari, Y.S Rao, formulation, evaluation and comparision of dissolution profiles of Eslicarbazepine acetate immediate release tablets using natural binders against synthetic binder, International Journal of Pharmacy and Pharmaceutical sciences, 2013, 5 (4):192-194.

18.Md Sarfaraz, V.G.Joshi, Immediate release solid oral dosage form of salbutamol sulphate:design, optimization and evaluation, International Journal of Pharmacy and Pharmaceutical sciences, 2013, 5 (4): 610-618.

19.Leon Lachmann , Herbert A , Liberman , Joseph L.Kaing , The theory and practice of Industrial Pharmacy:293-303.

20. Aulton`s Pharmaceutics, The design & manufacture of medicines, Biopharmaceutics and pharmacokinetics, A Treatise, second edition, Valabh Prakashan, 315-84.

21. Shirwaikar R., Shirwaikar A., Prabu L., Mahalaxmi R., Rajendran K., Kumar C. Studies of superdisintegrant properties of seed mucilage of Ocimum gratissimum. Indian Journal of Pharmaceutical science