AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Immediate Drug Release Dosage Form: A Review

Kiran Wale[1*], Kishor Salunkhe[2], Ishwar Gundecha[2], Mahesh Balsane[2], Snehal Hase[2], Priya Pande[2].

1.Amrutvahini College Of Pharmacy Sangamner,Ahmednagar,Maharashtra, India.

ABSTRACT

Over the past few decades, there has been an increased interest for innovative drug delivery systems to improve safety, efficacy and patient compliance, thereby increasing the product patent life cycle. There are novel types of dosage forms that act very quickly after administration. The basic approach used in development tablets is the use of superdisintegrants like Cross linked carboxymelhyl cellulose (Croscarmeliose), Sodium starch glycolate (Primogel, Explotab), Polyvinylpyrrolidone (Polyplasdone) etc. which provide instantaneous disintegration of tablet after administration. Immediate release liquid dosage forms and parenteral dosage form have also been introduced for treating patients. Liquid dosage form can be suspensions with typical dispersion agents like hydroxypropyl methylcellulose, AOT (dioctylsulfosuccinate) etc. The development of immediate release therapy also provides an opportunity for a line extension in the marketplace, A wide range of drugs (e.g., neuroleptics, cardiovascular drugs, analgesics, antihistamines, and drugs can be considered candidates for this dosage form. In this regard, immediate release formulations are similar to many sustained release formulations that are now commonly available. oral film dosage form not only has certain advantages of other fast disintegrating systems but also satisfies the unmet needs of the market. The present review emphasizes on the potential benefits, design and development of robust, stable, and innovative orally immediate and their future scenarios on a global market as a pharmaceutical dosage form.

Keywords: Immediate release, polymers, superdisintegrant.

*Corresponding Author Email: kiranwale81@gmail.com

Received 13 November 2013, Accepted 26 November 2013

Please cite this article in press as: Wale K. *et al.*, Immediate Drug Release Dosage Form: A Review. American Journal of PharmTech Research 2014.

INTRODUCTION

In the present research and study novel drug delivery systems are developed for expanding markets/indications, extending product life cycles and generating opportunities. Oral administration is the most popular route for systemic effects due to its ease of ingestion, pain, avoidance, versatility and most importantly, patient compliance. Also solid oral delivery systems do not require sterile conditions and are therefore, less expensive to manufacture**.** Patient compliance, high-precision dosing, and manufacturing efficiency make tablets the solid dosage form of choice. Excipients and equipments choices will be significantly affected should solid dosage form technologies change in response to the unprecedented shifts in the drug discovery such as genomics. The development of enhanced oral protein delivery technology by immediate release tablets which may release the drugs at an enhanced rate are very promising for the delivery of poorly soluble drugs high molecular weight protein and peptide. Injections generally are not favored for use by patients unless facilitated by sophisticated auto injectors. Inhalation is one good alternative system to deliver these drugs, but the increased research into biopharmaceuticals so far has generate predominantly chemical entities with low molecular weights. Many patients require quick onset of action in particular therapeutic condition and consequently immediate release of medicament is required. It is estimated that50% of the population is affected by this problem, which results in a high incidence of ineffective therapy.

Definition:- [1,3,7-9]

Immediate release dosage form are those which disintegrate rapidly and get dissolved to release the medicaments. Immediate release may be provided for by way of an appropriate pharmaceutically acceptable diluent or carrier, which diluent or carrier does not prolong, to an appreciable extent, the rate of drug release and/or absorption. This term excludes formulations which are adapted to provide for “modified”, “controlled”, “sustained”, “prolonged”, “extended” or “delayed” release of drug.

The term “ immediate release” pharmaceutical formulation includes any formulation in which the rate of release of drug from the formulation and/or the absorption of drug, is neither appreciably, nor intentionally, retarded by galenic manipulations. In the present case, immediate release may be provided for by way of an appropriate pharmaceutically acceptable diluent or carrier, which diluent or carrier does not prolong, to an appreciable extent, the rate of drug release and/or absorption. Thus, the term excludes formulations which are adapted to provide for “modified”, “controlled”, “sustained”, “prolonged”, “extended” or “delayed” release of drug.

Biopharmaceutic Consideration:[1-3,10,11]

Must that to consider Biopharmaceutical factor like metabolism and excretion.

Pharmacokinetics:

It is the meditation, study has done on absorption, distribution, metabolism and excretion. After absorption, drug attains therapeutic level and therefore elicits pharmacological effect, so both rate and extend of absorption is important. In conventional dosage form there is delay in disintegration and therefore dissolution is fast. Drug distribution depends on many factors like tissue permeability, perfusion rate, binding of drug to tissue, disease state, drug interaction etc.

Duration and intensity of action depends upon rate of drug removal from the body or site of action i.e. biotransformation. Decrease in liver volume, regional blood flow to liver reduces the biotransformation of drug through oxidation, reduction and hydrolysis. Excretion by renal clearance is slowed, thus half-life of renal excreted drugs increase.

Pharmacodynamic:

Drug reception interaction impaired in elderly as well as in young adult due to undue development of organ.

- Decreased sensitivity of -adrenergic agonist and antagonist.
- Decreased ability of the body to respond reflexive stimuli, cardiac output, and orthostatic hypotension may see in taking antihypertensive like prazosin.
- Altered response to drug therapy-elderly show diminished bronchodilator effect of theophylline shows increased sensitivity to barbiturates.
- Concomitant illnesses are often present in elderly, which is also taken into consideration, while multiple drug therapy prescribed.
- Immunity is less and taken into consideration while administered antibiotics.

Research workers have clinically evaluated drug combination for various classes' cardiovascular agents, diuretics, anti-hypertensive etc. for immediate release dosage forms. The combination choice depends on disease state of the patient.

Trouble with Existing Oral Dosage Form:[1,3,12,13]

- Patient may suffer from tremors therefore they have difficulty to take powder and liquids. In dysphasia physical obstacles and adherence to an oesophagus may cause gastrointestinal ulceration.
- Liquid medicaments (suspension and emulsion) are packed in multidose container; therefore achievement of uniformity in the content of each dose may be difficult.

- Swallowing of solid dosage forms like tablet and capsules and produce difficulty for young adult of incomplete development of muscular and nervous system and elderly patients suffer from dysphasia.
- Cost of products is main factor as parenteral formulations are most costly and discomfort.
- Buccal and sublingual formation may cause irritation to oral mucosa, so patients refused to use such medications.

Desired Criteria For Immediate Release Drug Delivery System: [1,3]

- Rapid dissolution and absorption of drug, which may produce rapid onset of action.
- Be manufactured using conventional processing and packaging equipment at low cost.
- Have a pleasing mouth feel.
- In the case of liquid dosage form it should be compatible with taste masking.
- Be portable without fragility concern.
- Exhibit low sensitivity to environmental condition as humidity and temperature.
- It should not leave minimal or no residue in the mouth after oral administration.
- In the case of solid dosage it should dissolve or disintegrate in the stomach within a short period.

Merits of Immediate Release Drug Delivery System: [15,1-3]

- ✓ Ability to provide advantages of liquid medication in the form of solid preparation.
- ✓ Adaptable and amenable to existing processing and packaging machinery .
- ✓ Improved compliance/added convenience .
- ✓ Improved stability, bioavailability .
- ✓ Suitable for controlled/sustained release actives .
- ✓ Allows high drug loading.
- ✓ Cost- effective .
- ✓ Decreased disintegration and dissolution times for immediate release oral dosage forms.
- ✓ Improved solubility of the pharmaceutical composition.
- ✓ There is no dose dumping problem.

POTENTIAL CRITERIA FOR IMMEDIATE RELEASE ORAL DOSAGE FORM. [1-3,15]

Anti-bacterial Agents:

Imipenem , nalidixic acid, nitro furantoin, rifampicin, spiramycin, sulphabenzamide, sulphadoxine, sulphamerazine, sulphacetamide, sulphadiazine, sulphafurazole, sulphamethoxazole, sulphapyridine, tetracycline, trimethoprim. Benethamine, penicillin, cinoxacin,ciprofloxacinHCl,clarithromycin,clofazimine,cloxacillin,demeclocycline, doxycycline,

erythromycin, ethionamide.

Anti-Arrhythmic Agents:

Amiodarone HCl, Disopyramide, flecainide acetate,quinidine sulphate.

Anti-depressants:

Amoxapine, ciclazindol, maprotiline HCl, mianserin HCl, nortriptyline HCl, trazodone HCl, trimipramine maleate.

Anti-coagulants:

Dicoumarol,dipyridamole, nicoumalone, phenindione.

Analgesics and Anti-inflammatory Agents:

Aloxiprin, auranofin,azapropazone, benorylate, diflunisal, etodolac, fenbufen, fenoprofen calcim, flurbiprofen, ibuprofen, indomethacin, ketoprofen, meclofenamic acid, mefenamicacid, nabumetone, naproxen, oxaprozin,oxyphenbutazone, phenylbutazone,piroxicam, sulindac.

Anthelmintics :

Albendazole, bephenium, hydroxynaphthoate , cambendazole, dichlorophen,ivermectin, mebendazole, oxamniquine, oxfendazole, oxantel embonate, praziquantel, pyrantel embonate, thiabendazole.

Anti-fungal Agents:

Amphotericin, butoconazolenitrate, clotrimazole, econazolenitrate, fluconazole, flucytosine,griseofulvin, itraconazole,ketoconazole, miconazole, natamycin, nystatin, sulconazole nitrate, terbinafine HCl, terconazole, tioconazole, undecenoic acid.

Anti-diabetics

Acetohexamide,chlorpropamide, glibenclamide,gliclazide, glipizide, tolazamide, tolbutamide,sitagliptin.

Anti-epileptics:

Beclamide, carbamazepine, clonazepam, ethotoin, methoin, methsuximide, methylphenobarbitone, oxcarbazepine, paramethadione,phenacemide, phenobarbitone,phenytoin, phensuximide, primidone, sulthiame, valproic acid.

Anti-hypertensive Agents:

Amlodipine, carvedilol, benidipine, darodipine, dilitazem HCl, diazoxide, felodipine, guanabenz acetate, indoramin, isradipine, minoxidil, nicardipine HCl, nifedipine, nimodipine, phenoxybenzamine HCl, prazosin HCL, reserpine, terazosin HCl.

Anti-gout Agents:

Allopurinol, probenecid, sulphinpyrazone.

Anti-malarials:

Amodiaquine, chloroquine, chlorproguanil HCl, halofantrine HCl, mefloquine HCl, proguanil HCl, pyrimethamine, quinine sulphate.

Anti-migraine Agents:

Dihydroergotamine mesylate,ergotamine tartrate, methysergidemaleate, pizotifen maleate, sumatriptan succinate.

Anti-muscarinic Agents:

Atropine, benzhexol HCl,biperiden, ethopropazine HCl, hyoscine butyl bromide, hyoscyamine, mepenzolate bromide,orphenadrine, oxyphencylcimineHCl, tropicamide.

Anxiolytic, Sedatives, Hypnotics and Neuroleptics:

Alprazolam, amylobarbitone, barbitone, bentazepam, bromazepam, bromperidol, brotizolam, butobarbitone, carbromal, chlordiazepoxide chlormethiazole, chlorpromazine, clobazam, clotiazepam,clozapine, diazepam, droperidol,ethinamate, flunanisone, flunitrazepam, fluopromazine, flupenthixol decanoate, fluphenazine decanoate, flurazepam, haloperidol.

Anti-protazoal Agents:

Benznidazole, clioquinol, decoquinate, diiodohydroxyquinoline, diloxanide furoate, dinitolmide, furzolidone, metronidazole, nimorazole, nitrofurazone, omidazole, tinidazole.

Anti-thyroid Agents: Carbimazole, propylthiouracil.

Anti-neoplastic Agents and Immunosuppressants:

Aminoglutethimide, amsacrine, azathioprine, busulphan, chlorambucil, cyclosporin, dacarbazine, estramustine, etoposide, lomustine, melphalan, mercaptopurine, methotrexate, mitomycin, mitotane, mitozantrone, procarbazine HCl, tamoxifen citrate, testolactone.

Anti-protazoal Agents:

Benznidazole, clioquinol,decoquinate,diiodohydroxyquinoline,diloxanide furoate, dinitolmide, furzolidone, metronidazole, nimorazole, nitrofurazone, omidazole, tinidazole.

Diuretics:

Acetazolamideamiloride, bendrofluazide, bumetanide, chlorothiazide, chlorthalidone, ethacrynic acid,frusemide, metolazone, spironolactone, triamterene.

Corticosteroids:

Beclomethasone , betamethasone , budesonide,cortisone acetate, desoxymethasone, dexamethasone, fludrocortisoneacetate, flunisolide, flucortolone,fluticasone propionate, hydrocortisone, methylprednisolone, prednisolone,prednisone, triamcinolone.

Cardiac Inotropic Agents:

Amrinone, digitoxin,digoxin, enoximone, lanatoside C, medigoxin.

Nitrates and other Anti-anginal Agents:

Amyl nitrate, glyceryltrinitrate, isosorbide dinitrate, isosorbide mononitrate, pentaerythritol tetranitrate.

NutritionalAgents:

Betacarotene, vitamin A, vitamin B2, vitamin D,vitamin E, vitamin K.Opioid .

Analgesics:

codeine, dextropropyoxyphene, diamorphine,dihydrocodeine, meptazinol,methadone, morphine, nalbuphine, pentazocine.

Oral Vaccines:

Vaccines designed to prevent or reduce the symptoms of diseases of which the following is a representative Influenza, Tuberculosis, Meningitis, Hepatitis, Whooping Cough, Polio, Tetanus, Diphtheria, Malaria, Cholera, Herpes, Typhoid, HIV, AIDS, Measles, Lyme disease, Travellers Atrophic rhinitis, Erysipelas, Foot and Mouth disease, Swine, pneumonia, and other disease conditions and other infections and auto-immune disease conditions affecting companion and farm animals.etc.

Proteins, Peptides and Recombinant drugs:

Insulin, glucagon, growth hormone (somatotropin),polypeptides or their derivatives, calcitonins and synthetic modifications thereof, enkephalins, interferons, LHRH and analogues (nafarelin, buserelin, zolidex), GHRH, secretin, bradykin antagonists, GRF, THF,TRH, ACTH analogues, IGF (insulin like growth factors),CGRP(calcitoningene related peptide), a trial natriurecticpeptide, vasopressin and analogues(DDAVP, lypressin),factor VIII, G-CSF (granulocyte-colony stimulating factor), EPO (erythropoitin).

Enzymes: All the enzymes.

Anti-parkinsonian Agents:

Bromocriptine mesylate, lysuride maleate.

Gastro-intestinal Agents:

Bisacodyl, cimetidine, cisapride, diphenoxylate HCl, domperidone, famotidine, loperamide, mesalazine, nizatidine, omeprazole, ondansetron HCL, ranitidine HCl, sulphasalazine .

Histamine H,-Receptor Antagonists:

Acrivastine, astemizole, cinnarizine, cyclizine, cyproheptadine HCl, dimenhydrinate, flunarizine HCl,loratadine, meclozine HCl, oxatomide, terfenadine, triprolidine.

Lipid Regulating Agents:

Bezafibrate, clofibrate, fenofibrate, gemfibrozil, probucol.

Local Anesthetics : Lidocaine

Neuro-muscular Agents: Pyridostigmine.

Spermicides: Nonoxynol.

Stimulants:

Amphetamine, dexamphetamine, dexfenfluramine, fenfluramine, mazindol, pemoline.

Sex Hormones:

Clomiphenecitrate, danazol, ethinyloestradiol, medroxy progesterone acetate, mestranol , methyltestosterone, norethisterone, norgestrel, oestradiol, conjugated oestrogens, progesterone, stanozolol, stiboestrol, testosterone, tibolone.

EXCIPIENTS USE IN IMMEDIATE RELEASE DOSAGE FORM: [1,2,3,8,18]

Excipients balance the properties of the actives in immediate release dosage forms. This demands a thorough understanding of the chemistry of these excipients to prevent interaction with the actives. Determining the cost of these ingredients is another issue that needs to be addressed by formulators. The role of excipients is important in the formulation of fast-melting tablets. These inactive food-grade ingredients, when incorporated in the formulation, impart the desired organoleptic properties and product efficacy. Excipients are general and can be used for a broad range of actives, except some actives that require masking agents.

Bulking materials:

Bulking materials are significant in the formulation of fast-melting tablets. The material contributes functions of a diluent, filler and cost reducer. Bulking agents

improve the textural characteristics that in turn enhance the disintegration in the mouth, besides; adding bulk also reduces the concentration of the active in the composition. The recommended bulking agents for this delivery system should be more sugar-based such as mannitol, polydextrose, lactitol, DCL (direct compressible lactose) and starch hydrolystate for higher aqueous solubility and good sensory perception. Mannitol in particular has high aqueous solubility and good sensory perception. Bulking agents are added in the range of 10 percent to about 90 percent by weight of the final composition .

Emulsifying agents:

Emulsifying agents are important excipients for formulating immediate release tablets they aid in rapid disintegration and drug release. In addition, incorporating emulsifying agents is useful in stabilizing the immiscible blends and enhancing bioavailability. A wide range of emulsifiers is recommended for fast-tablet formulation, including alkyl sulfates, propylene glycol esters,

lecithin, sucrose esters and others. These agents can be incorporated in the range of 0.05 percent to about 15 percent by weight of the final composition.

Lubricants:

Lubricants, though not essential excipients, can further assist in making these tablets more palatable after they disintegrate in the mouth. Lubricants remove grittiness and assist in the drug transport mechanism from the mouth down into the stomach.

Flavours and sweeteners:

Flavours and taste-masking agents make the products more palatable and pleasing for patients. The addition of these ingredients assists in overcoming bitterness and undesirable tastes of some active ingredients. Both natural and synthetic flavours can be used to improve the organoleptic characteristic of fast-melting tablets. Formulators can choose from a wide range of sweeteners including sugar, dextrose and fructose, as well as non-nutritive sweeteners such as aspartame, sodium saccharin, sugar alcohols and sucralose. The addition of sweeteners contributes a pleasant taste as well as bulk to the composition.

Superdisintegrants: [19]

Disintegrating agents are substances routinely included in the tablet formulations to aid in the breakup of the compacted mass when it is put into a fluid environment. They promote moisture penetration and dispersion of the tablet matrix. In recent years, several newer agents have been developed known as "Superdisintegrants". These newer substances are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. On contact with water the superdisintegrants swell, hydrate, change volume or form and produce a disruptive change in the tablet. Effective superdisintegrants provide improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high-dose drugs.

Selection Criteria for Superdisintegrant:

Although superdisintegrants primarily affect the rate of disintegration, but when used at high levels it can also affect mouth feel, tablet hardness and friability. Hence, various ideal factors to be considered while selecting an appropriate superdisintegrants for a particular formulation should:

1. Proceed for rapid disintegration, when tablet comes in contact with saliva in the mouth/oral cavity.
2. Be compactable enough to produce less friable tablets.

3. Produce good mouth feel to the patients. Thus, small particle size is preferred to achieve patient compliance.
4. Have good flow, since it improves the flow characteristics of total blend.

TYPES OF SUPERDISINTEGRANTS:- [1,2,3,19]

The Superdisintegrants can be classified into two categories on the basis of their availability:

- Natural superdisintegrant
- Synthetic superdisintegrant

Natural superdisintegrant:

These superdisinegrating agents are natural in origin and are preferred over synthetic substances because they are comparatively cheaper, abundantly available, non-irritating and nontoxic in nature. The natural materials like gums and mucilages have been extensively used in the field of drug delivery for their easy availability, cost effectiveness, Eco friendliness, emollient and non-irritant nature, non-toxicity, capable of multitude of chemical modifications, potentially degradable and compatible due to natural origin. There are several gums and mucilages are available which have super-disintegrating activity

1) Plantago Ovata Seed Mucilage (Isapgula)
2) Lepidiumsativum Mucilage
3) Gum Karaya
4) Fanugreek Seed Mucilage
5) Cassia fistula gum
6) Locust Bean gum
7) Hibiscus rosa-sinensis Linn. Mucilage
8) Mango Peel Pectin
9) Lallemantia reylenne seeds
10) Aegle marmelos gum (AMG)
11) Ficus indica fruit mucilage
12) Dehydrated banana powder (DBP)

SYNTHETIC SUPERDISINTEGRANTS:

A group of superdisintegrants including croscamellose sodium (Ac-Di-Sol) sodium starch glycolate (Primojeland Explotab) and crospovidone (Polyplasdone XL) alleviate most of these problems. Use of the superdisintegrants in fast dispersible tablet is possible as tablet shows optimum physical properties.

Advantages of Synthetic Superdisintegrants:

- Effective in lower concentrations than starch.
- Less effect on compressibility and flow ability.
- More effective intragranularly.

Some super disintegrants are:

1. **Cross-linked Povidone (crospovidone) (Kollidone)** used in concentration of 2-5% of weight of tablet. Completely insoluble in water.

Mechanism of Action:

Water wicking, swelling and possibly some deformation recovery. Rapidly disperses and swells in water, but does not gel even after prolonged exposure. Greatest rate of swelling compared to other disintegrants. Greater surface area to volume ratio than other disintegrants.

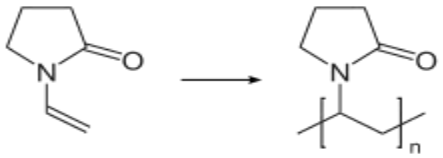

Figure 1.Cross-linked Povidone (crospovidone)

Sodium Starch Glycolate (Explotab, primogel) used in concentration of 2-8 % & optimum is 4%.

Mechanism of Action:

Rapid and extensive swelling with minimal gelling. Microcrystalline cellulose (Synonym: Avicel, celex) used in concentration of 2-15% of tablet weight. And Water wicking.

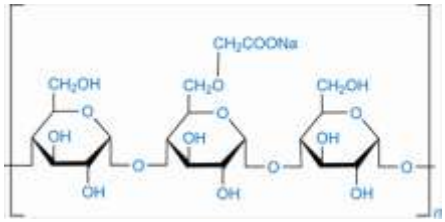

Figure 2. Sodium Starch Glycolate (Explotab, primogel)

Cross linked carboxy methyl cellulose sodium (i.e. Ac-Di-sol) Croscarmellose sodium:

Mechanism of Action:

Wicking due to fibrous structure, swelling with minimal gelling. Effective Concentrations: 1-3% Direct Compression, 2-4% Wet Granulation.

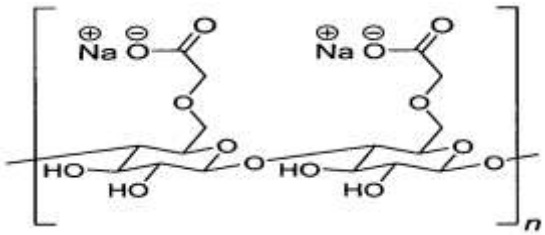

Figure 3.Cross linked carboxy methyl cellulose sodium

Low-substituted hydroxyl propyl cellulose, which is insoluble in water. Rapidly swells in water. Grades LH-11 and LH-21 exhibit the greatest degree of swelling. Certain grades can also provide some binding properties while retaining disintegration capacity. Recommended concentration 1-5%.

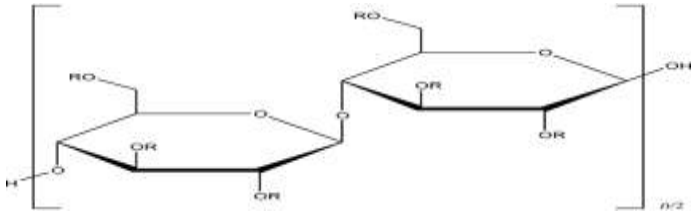

Figure 4.Low-substituted hydroxyl propyl cellulose

Technique Used In The Preparation of Immediate Release Tablets:-[1-3,26]

1. Tablet molding technique
2. Wet granulation technique
3. Direct compression technique
4. By solid dispersions
5. Mass extrusion technique

Tablet Molding Technique :

In this method, water-soluble ingredients are used so that tablet disintegrate and dissolve rapidly. The powder blend is moistened with a hydro alcoholic solvent and is molded in to tablet using compression pressure lower than used in conventional tablets compression. The solvent is then removed by air-drying. Molded tablets have a porous structure that enhances dissolution. Two problems commonly encountered are mechanical strength and poor taste masking characteristics. Using binding agents such as sucrose, acacia or poly vinyl pyrrolidone can increase the mechanical strength of the tablet. To overcome poor taste masking characteristic Van Scoik incorporated drug containing discrete particles, which were formed by spray congealing a molten mixture of hydrogenated cottonseed oil, sodium bicarbonate, lecithin, polyethylene glycol and active ingredient into a lactose based tablet triturate form.

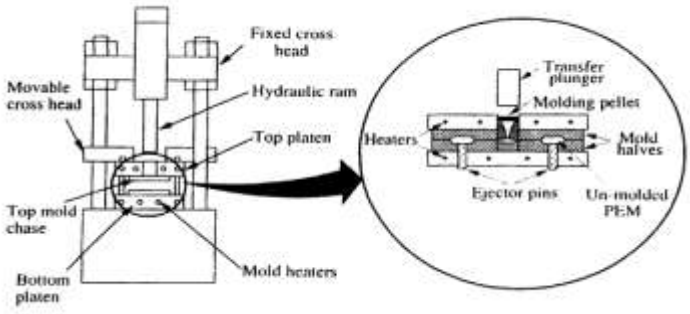

Figure 5. Tablet Molding Technique

2. Wet granulation technique:

Wet granulation is a process of using a liquid binder to lightly agglomerate the powder mixture. The amount of liquid has to be properly controlled, as over-wetting will cause the granules to be too hard and under-wetting will cause them to be too soft and friable. Aqueous solutions have the advantage of being safer to deal with than solvent-based systems but may not be suitable for drugs which are degraded by hydrolysis.

i. The active ingredient and excipients are weighed and mixed.

ii. The wet granulate is prepared by adding the liquid binder–adhesive to the powder blend and mixing thoroughly. Examples of binders/adhesives include aqueous preparations of cornstarch, natural gums such as acacia, and cellulose derivatives such as methyl cellulose, gelatin, and povidone.

iii. Screening the damp mass through a mesh to form pellets or granules.

iv. Drying the granulation. A conventional tray-dryer or fluid-bed dryer are most commonly used.

v. After the granules are dried, they are passed through a screen of smaller size than the one used for the wet mass to create granules of uniform size.

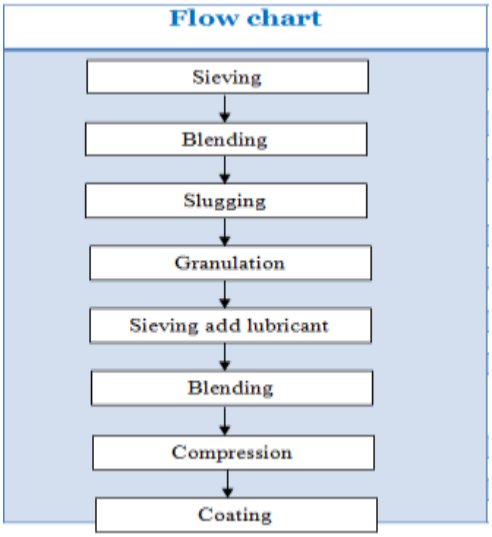

Figure 6. Wet granulation technique

Low shear wet granulation processes use very simple mixing equipment, and can take a considerable time to achieve a uniformly mixed state. High shear wet granulation processes use equipment that mixes the powder and liquid at a very fast rate, and thus speeds up the manufacturing process. Fluid bed granulation is a multiple-step wet granulation process performed in the same vessel to pre-heat, granulate, and dry the powders. It is used because it allows close control of the granulation process.

3.Direct compression technique:

In this method, tablets are compressed directly from the mixture of the drug and excipients without any preliminary treatment. The mixture to be compressed must have adequate flow properties and cohere under pressure thus making pretreatment as wet granulation unnecessary. Few drugs can be directly compressed into tablets of acceptable quality. A type of disintegrant and its proportion are of prime importance. The other factors to be considered are particle size distribution, contact angle, pore size distribution, tablet hardness and water absorption capacity. All these factors determine the disintegration. The disintegrant addition technology is cost effective and easy to implement at industrial level.

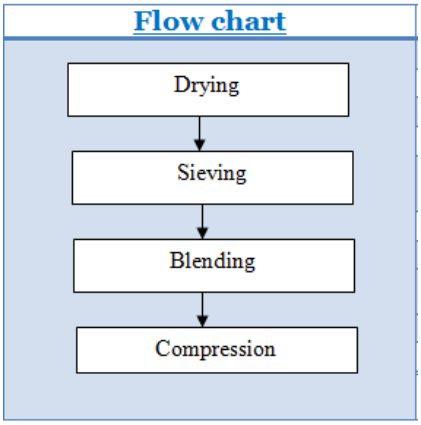

Figure 7. Direct compression technique

4. Solid dispersions technique: [26]

When formulating such solid amorphous dispersions into immediate release solid dosage forms for oral administration to a use environment such as the GI tract of an animal such as a human, it is often desirable to maximize the amount of dispersion present in the dosage form. This minimizes the size of the solid dosage form required to achieve the desired dose. Depending on the drug dose, it is often desired that the solid amorphous dispersion comprise at least 30 wt %, preferably at least wt %, and more preferably at least 50 wt % or more of the solid dosage form. Such high drug loadings of dispersion in a solid dosage form minimize the dosage form's size, making it easier for the patient to swallow it and tending to improve patient compliance.

The drug dispersions used in fabricating the high loading immediate release dosage forms of the present invention comprise solid dispersions of a drug and at least one concentration-enhancing polymer. The concentration-enhancing polymer is present in the dispersions used in the present invention in a sufficient amount so as to improve the concentration of the drug in a use environment relative to a control composition. At a minimum, the dispersions used in the present invention provide concentration enhancement relative to a control consisting of crystalline drug

alone. Thus, the concentration-enhancing polymer is present in a sufficient amount so that when the dispersion is administered to a use environment, the dispersion provides improved drug concentration relative to a control consisting of an equivalent amount of crystalline drug, but with no concentration-enhancing polymer present.

The immediate release dosage forms containing a solid dispersion that enhances the solubility of a "low-solubility drug," meaning that the drug may be either "substantially water-insoluble," which means that the drug has a minimum aqueous solubility at physiologically relevant pH (e.g., pH 1-8) of less than 0.01 mg/mL, "sparingly water-soluble," that is, has an aqueous solubility up to about 1 to 2 mg/mL, or even low to moderate aqueous-solubility, having an aqueous-solubility from about 1 mg/mL to as high as about 20 to 40 mg/mL.

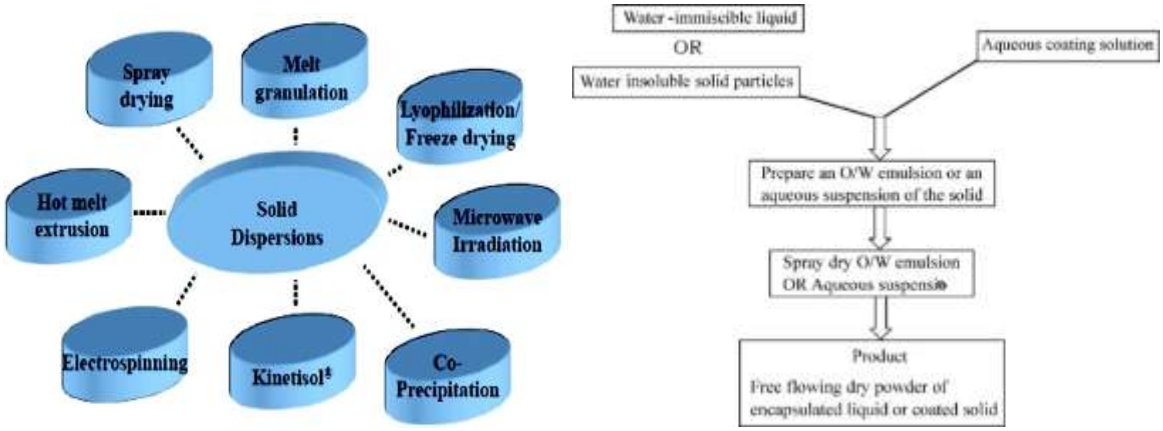

Figure 8. solid dispersions technique

5. Mass extrusion technique:

This technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol and subsequent expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules for bitter drugs and thereby achieve taste masking.

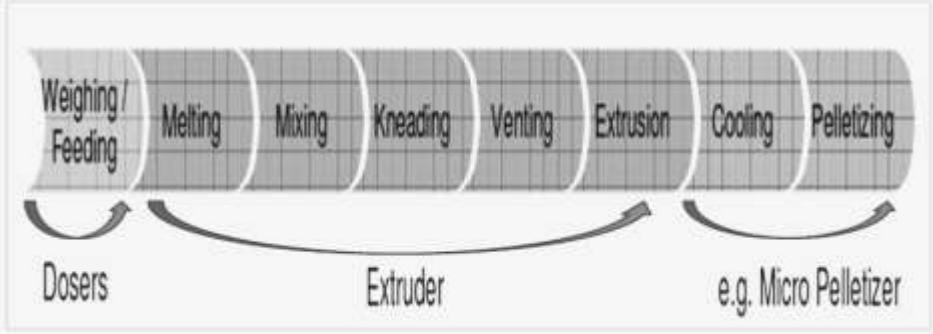

Figure 9.Mass extrusion technique

EVALUATION OF IMMEDIATE RELEASE TABLETS DOSAGE FORM: [29,3,1]

I. Evaluation of Blend:

The prepared blend is evaluated by following tests.

A. Angle of repose

B. Tapped density

C. Bulk density

D. Carr's index

E. Hauser's ratio

A. Angle of repose:

Angle of repose was determined by using funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in sucha way that the tip of the funnel just touches the apex of the heap of blend. The drug excipient blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

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

Here;

h = Height of pile

r = Radius of pile

θ = Angle of repose

B. Tapped density:

Tapped density is ratio of mass of tablet blend to tapped volume of tablet blend. Accurately weighed amount of tablet blend poured in graduated cylinder and height is measured. Then cylinder was allowed to 100tap under its own weight onto a hard surface. The tapping was continued until no further change in height was noted.

$$Tapped\ Density(V_t) = \frac{Mass}{TappedVolu\ me}$$

C. Bulk density:

Bulk density was determined by pouring a weighed quantity of tablet blend into graduated cylinder and measuring the height. Bulk density is the ratio of mass of tablet blend to bulk volume.

$$Bulk\ Density(V_b) = \frac{Mass}{Bulk\ Volume}$$

D. Carr's index:

Compressibility is the ability of powder to decrease in volume under pressure using bulk density and tapped density the percentage compressibility of powder were determined, which is given as carr's compressibility index. It is indirectly related to the relative flow rate. Carr's compressibility index was determined by the given formula.

$$Carr's\ Index(I) = \frac{V_t - V_b}{V_t} \times 100$$

E. Hauser's ratio:

Hausner's ratio indicates the flow properties of powder and measured by the ratio of tapped density to bulk density. Hausner's ratio was determined by the given formula.

$$\text{Hauser's ratio} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

EVALUATION OF TABLETS:- [2,3,28]

The tablets quality control tests following:

1. Appearance
2. Thickness
3. Hardness
4. Weight variation
5. Friability
6. Disintegration
7. Uniformity of dispersion
8. Wetting Time
9. Water absorption ratio
10. Drug content
11. Taste / Mouth feel
12. *In vitro* Dissolution
13. Stability studies

1. Appearance:

The general appearance of tablet is its visual identity and all over elegance, shape, color, surface textures. These all parameters are essential for consumer acceptance.

2. Thickness:

The thickness of the tablets was determined by using vernier calipers. Randomly 10 tablets selected were used for determination of thickness that expressed in Mean± SD and unit is mm.

3. Hardness:

The hardness of tablet is an indication of its strength against resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling before usage. Measuring the force required to break the tablet across tests it. Hardness of 10 tablets (randomly) from whole tablet batch was determined by Monsanto hardness tester. Hardness measured in kg/cm2.

4. Weight variation:

The weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. The total weight of 20 tablets randomly from whole batch was determined and the average was calculated. The individual weights of the tablets were also determined accurately and the weight variation was calculated.

5. Friability test:

Friability is the loss of weight of tablet in the container due to removal of fine particles from the surface during transportation or handling. Roche friabilator was employed for finding the friability of the tablets. For tablets with an average weight of 0.65 g or less take a sample of whole tablets corresponding to about 6.5 g and for tablets with an average weight of more than 0.65 g take a sample of 10 whole tablets. Roche friabilator is rotated at 25rpm for 4 minutes for 100rounds. The tablets were dedusted and weighed again. The percentage of weight loss was calculated using the formula.

$$F(\%) = \frac{(W_{initial}) - (W_{final})}{(W_{initial})} X\ 100$$

Here, %f = Percentage friability

W0 = Initial weight (Before test)

W1 = Final weight (After test)

6. Disintegration test:

The USP device to rest disintegration was six glass tubes that are “3 long, open at the top, and held against 10” screen at the bottom end of the basket rack assembly. One tablet is placed in each tube and the basket rack is poisoned in 1 liter beaker of distilled water at 37± 20C, such that the tablets remain below the surface of the liquid on their upward movement and descend not closer than 2.5cm from the bottom of the beaker.

7. Uniformity of dispersion:

Two tablets were kept in 100ml water and gently stirred for 2 minutes. The dispersion was passed through 22 meshes. The tablets were considered to pass the test if no residue remained on the screen.

8. Wetting Time:

The wetting time of the tablets was measured using a simple procedure. Five circular tissue papers of 10cm diameter were placed in a petridish containing 0.2% w/v solution of amaranth (10ml). One tablet was carefully placed on the surface of the tissue paper. The time required for develop blue color due to amaranth water soluble dye on the upper surface of the tablets was noted as the wetting time.

9. Water Absorption Ratio:

A small piece of tissue paper folded twice was placed in a small petridish containing 6ml of water. A tablet was put on the paper. The wetted tablet was then weighed. Water absorption ratio, R was determined by using following formula.

$$R = \frac{W_a - W_b}{W_a} \times 100$$

Here, R = Water absorption ratio

Wb = Weight of tablet before water absorption

Wa = Weight of tablet after water absorption

10. Drug content:

10 tablets were powdered and 100mg drug equivalent powder dissolved in suitable media buffer or 0.1N HCl. Volume of the solution made up to 100ml by that media. Solution was filtered and diluted 100times and analyzed spectrophotometrically and further calculation carried out to determine drug content in one tablet.

11. In vitro drug release studies:

The immediate release tablets are subjected to in vitro drug release studies in pH 6.8 phosphate buffer or 0.1N HCl for 30 minutes to access the ability of the formulation for providing immediate drug delivery.

Drug release studies were carried out in dissolution test apparatus using specified volume 900ml of dissolution media maintained at 37±0.20C. The tablets are kept in the cylindrical basket or directly placed in medium with paddle then rotated at 100 rpm. 5ml of the sample from the dissolution medium are withdrawn at each time interval (5, 10, 15 & 30 minutes) and 5ml of

fresh medium was replaced each time. The samples were filtered and from the filtrate 1ml was taken and diluted to 10ml. These samples were analyzed spectrophotometrically and further calculation was carried out to get drug release. The drug released data were plotted and tested with zero order (Cumulative % drug released Vs time), First order (Log % Remained Vs time). The in vitro dissolution kinetic parameters, dissolution rate constants, correlation coefficient and dissolution efficiency were calculated.

12. Stability study:

Stability is defined as the ability of a particular drug or dosage form in a specific container to remain within its physical, chemical, therapeutic, and toxicological specifications. Drug decomposition or degradation occurs during storage, because of chemical alteration of the active ingredients or due to product instability, lowering the concentration of the drug in the dosage form. Stability study of the dosage form must include a section for product characterization and another section to study the product stability during storage. Formulations are evaluated for their appearance, possible weight gain in drug content thickness, flatness, folding endurance, tensile strength, moisture content and moisture uptake, and in-vitro release study by keeping dosage form in different temperature and humidity condition after a specified time. The stability study indicates that the formulation is quite stable at different conditions of storage.

CONCLUSION:-

The demand for immediate release technology is rapidly growing to create a new tomorrow, as a revolutionary and an innovative dosage forms for all age groups, specifically pediatric, geriatric patients and patients with swallowing difficulties. A number of active ingredients including over the counter (OTC) products, prescription drugs and neutraceuticals, can be incorporated into this innovative immediate release dosage form. few companies are actively engaged in development of this fast pace, oral thin film technology, which allows brand extension for products and a good tool for product life cycle management for increasing the patent life of existing products. These tablets are designed to release the medicaments with an enhanced rate. Due to the constraints of the current technologies as highlighted above, there is an unmet need for improved manufacturing processes for immediate release pharmaceutical form that are mechanically strong, allowing ease of handling and packaging and with production costs similar to that of conventional tablets. To fulfill these medical needs, formulators have devoted considerable effort to developing a novel type of tablet dosage form for oral administration, one that disintegrates and dissolves rapidly with enhanced dissolution. An extension of market

exclusivity, which can be provided by a immediate release dosage form, leads to increased revenue, while also targeting underserved and under-treated patient populations.

REFERENCES:-

1. Nyol Sandeep, Dr. M.M. Gupta. Immediate Drug Release Dosage Form: A Review. J Drug Delivery & Therapeutics; 3(2), 155-161, 2013.
2. Rishikesh, Mohiuddin Ahmed Bhuyian, Ms.Irin Dewan, Drishti Rani Ghosh & Md.Asraful Islam. Immediate Release Drug Delivery System (Tablets): AN OVERVIEW. Int. Res J Pharm. App Sci; 2012;2(5):88-94.
3. Utsav Patel, Khushbu Patel, Darshan Shah, Rushabh Shah. A Review On Immediate Release Drug Delivery System. Int J Pharma Res And Biosci 2012; (5) :37-66.
4. Leon Lachman, Herbert A, Liberman and Joseph L. Kaing: The Theory And Practice of Industrial Pharmacy: 293-303.
5. Aulton`S Pharmaceutics, The Design & Manufacture Of Medicines, Biopharmaceutics And Pharmacokinetics, A Treatise, Second Edition, Vallabh Prakashan, 315-384.
6. Ansel`S Pharmaceutical Dosage Forms & Drug Delivery Systems, Eighth Edition, 227-260.
7. Dedhiya: Lercanidipine Immediate Release Compositions" United States Patent Application 20060134212.
8. Eriksson: New Oral Immediate Release Dosage Form" United States Patent Application 20060034 911.
9. Alami: Immediate Release Pharmaceutical Formulation, United States Patent Application 20060014734
10. Debjit Bhowmik, Chiranjib B, Krishnakanth, Pankaj R and Margret Chandira. Margret Chandira. R., Jayakar B, Pasupathi, A. Chakrabarty and BL Maruya P: Design, Development and Evaluation of Immediate Release Atorvastatin and Sustained Release Gliclazide Tablets J Pharm Res 2009; 6(2).
11. Fast Dissolving Tablet: An Overview, Journal of Chemical and Pharmaceutical Research, 2009, 1(1): 163-177.
12. Susijit Sahoo, B. Mishra, PIK. Biswal, Omprakash Panda, Satosh Kumar Mahapatra and Goutam Kumar Jana: Fast Disslving Tablet: As A Potential Drug Delivery System, Drug Invention Today 2010; (2): 130-133.

13. Jon Gabrielsson, Nils-Ol of Lindberg and Torbjorn Lundstedt, Multivariate Methods in Pharmaceutical applications, J. Chemom 2002; 16: 141-160.
14. Reddy LH: Fast Dissolving Drug Delivery Systems: A Review Of The Literature, IJPS. 2002: 331-336.
15. Sekar V and Chellan VR: Immediate Release Tablets of Telmisartan Using Superdisintegrant-Formulation, Evaluation and Stability Studies. Chem Pharm Bull(Tokyo). 2008; 56(4): 575-577.
16. B.G. Shiyani, R.B. Dholakiyal, B.V. Akbari, D.J. Lodhiyal and G.K. Ramani: Development and Evaluation of Novel Immediate Release Tablets of Metoclopramide HCI By Direct Compression Using Treated Gellan Gum As Disintegration-Accelerating Agent. J Pharm Res 2009; 2(9): 1460- 1464.
17. Jinjiang Li and Xiaohui Mei, Applications of Cellulose and Cellulose Derivatives In Immediate Release Solid Dosage ACS Symposium Series, Polysaccharides For Drug Delivery Pharma Applications. 19-55.
18. Mohit Mangal, Sunil Thakral, Manish Goswami, Pankaj Ghai. Superdisintegrants: An Updated Review. Int J Pharm Pharma Sci Res 2012; 2(2) 26-35.
19. Rangole US et al. Formulation and in-vitro evaluation of rapidly disintegrating tablets using hydrochlorothiazide as a model drug. Res J. Pharm. Tech Dec 2008; 1(4): 349-352.
20. Ghosh T et al. A Review on new generation orodispersible tablets and its future prospective. Int J Pharm Pharma Sci 2011; 3(1): 1-7.
21. Dhakane K et al. Fast dissolving tablet: A Future prospective. Journal of Pharmacy Research 2011; 4(11): 4176-4180.
22. Shekhar RS et al. Recent Trends of Oral Fast Disintegrating Tablets - An Overview of Formulation and Taste Masking Technology. Res J Pharma Biological Chemical Sci March 2012; 3(1): 771-793.
23. Kumar PT et al. Formulation and Evaluation of Film Coated Tilcopidine Hydrochloride Immediate Release Tablets. Int Res J Pharm 2012, 3 (5), 469-472.
24. Karimban JA et al. "Formulation and Evaluation of Immediate Release Venlafaxine HCl Tablets: Comparative Study of Super Disintegrant and Diluents" Int Res J Pharm 2012, 3 (4), 324-329.
25. Vaishnani R et al. Formulation and evaluation of immediate release tablets of paroxetine HCl using different superdisintegrants. Int J Res Pharma Biomedical Sci 2011; 2(3): 1095-1099.

26. W. L. Chiou, and S. Riegelman. Pharmaceutical applications of solid dispersion systems. J. Pharm. Sci 1971;60(9): 1281-1302.
27. Margret Chandira R and Jaykar B: Formulation and Evaluation of Orodispersible Tablets of Terbutaline Sulphate, Drug Invention Today 2010; 2(1):31-33.
28. Rakesh Patel and Ajay Suthar: Formulation and Process Optimization of Cinnarizine Fast-Release Tablets. Pharmaceutical Technology. 33(8): 53- 59.
29. Luber et al, Immediate release tablet, United States Patent 7323192.
30. Luber et al, Immediate release tablet, United States Patent 20080095845.
31. Thosar et al, Immediate release eplerenone compositions United States Patent 6410054 .
32. Forsman et al, Immediate release tablet, United States Patent 6521253 .
33. United States Patent Application 20030224043 .
34. Mehta et al, Raloxifene Immediate release tablet, United States Patent 20100003319.