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Review Article

MELT EXTRUSION – AN OVERVIEW

Sadhna khatry*[1], k. Abbulu[2]
[1]Sadhna khatry, Director, Dev Bhoomi Institute of Pharmacy and Research, Manduwala, Dehradun, Uttarakhand.
[2]Dr. k. Abbulu, Principal, Malla Reddy Institute of Pharmaceutical Sciences,
Kompally, Hyderabad, Andhra Pradesh.
Email: sadhna_khatry@yahoo.com

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ABSTRACT

Extrusion processing has been a preferred mode of fabrication in the plastics industry for nearly a century. Interest in the pharmaceutical applications is growing rapidly and is evident from the increasing number of patents and publications. Hot melt extrusion is a well recognized technology in pharmaceutical industry today and is used in the preparation of variety of dosage forms and drug delivery systems. The types of extruders currently available for hot melt extrusion are single and twin-screw extruders. Depending on the geometric design and function, the screw is generally composed of three different sections: feeding section, melting section, and the metering section. This paper highlights the advantages, applications of hot melt extrusion technology and the optimization of HME process through which product quality and performance is assured. Equipment parameters like screw configuration and screw speed, process parameters like temperature, melt viscosity, flow and melt pressure and the formulation parameters like physicochemical properties of the polymer and drug, drug-polymer miscibility and compatibility, glass transition temperature of the polymers, type of plasticizer and the desired drug release from dosage forms have a strong impact on the product and its performance. Optimization of HME process by proper selection of polymers, plasticizers, processing conditions and parameters plays a crucial role in the product performance.

Key words: Hot Melt Extrusion, Solid dispersions, Solubility enhancement; Thermal analysis, Glass transition temperature, Solubility parameters, Rheology, Sustained release.

INTRODUCTION

The word 'extrusion' is derived from the Latin 'extrudere', which literally means to press out or to drive out. Extrusion is the process of converting a raw material into a product of uniform shape and density by forcing it through a die under controlled conditions. Industrial applications of extrusion process dates back to 1930s[1]. The extrusion process was invented for the manufacturing of lead pipes by Joseph Brama at the end of the 18th century[2]. Currently, more than 50 % of all plastic products, including plastic bags, sheets and pipes are manufactured by this process[2]. Hot melt extrusion is not only used in the production of the polymeric articles but also in polymer production and compounding. Melt extrusion technique has found its place in the array of the pharmaceutical manufacturing operations which is evident from the increasing number of patents and publications in the scientific literature with over 100 papers published in the last 12 years[1]. Hot melt extrusion is mainly used to produce homogenous matrix formulations of the drug[4].

HME differs from simple extrusion in that, polymer, drug and excipient blends are mixed thoroughly in the molten state in this process, needing no solvents for granulation. The molten polymer serves as the thermal binder. Simple extrusion process uses aqueous or organic solvents for wetting the powder blend for granulation. It is a time consuming process since drying step is critical. Use of solvents in this process may degrade the drug and residual solvents may be present after drying. This process is used commonly in the preparation of the dosage forms and drug delivery systems. These dosage forms are complex mixtures of active medicaments, functional excipients and the processing aids[3].

ADVANTAGES

Hot melt extrusion technology has recently attracted much attention in the pharmaceutical field due to its advantages over traditional processing methods. Excellent mixing and agitation during processing cause suspended drug particles to deaggregate in the molten polymer and this results in extruded formulations with good content uniformity (99%-101%). It is an environmental friendly process, using no solvents and hence having no toxicological problems. It avoids the degradation problems which may be caused by the presence of solvents thereby resulting in improved stability. This process has potential for automation, since it is fast and a continuous

manufacturing process. Various stages in the process are integrated in one machine and time consuming drying step is eliminated. Poorly compactable materials can be easily formulated into tablets thereby eliminating tabletting problems. The process and formulation parameters can be controlled by using suitable polymers for achieving desired release profiles like sustained and controlled release. Minimum residence time in the process and short thermal exposure of the active pharmaceutical ingredients (API) allows the processing of thermo labile drugs. It is the best processing technique for improving the bioavailability of the poorly soluble drugs by forming solid dispersions and solutions. Medium to high load of API (>50%) is possible with this technique. High out-puts on the commercial scale (>500 kg/hr) are possible[2, 5].

PROCESS AND EQUIPMENT

The equipment consists of an extruder, downstream auxiliary equipment and other tools for monitoring the performance and product quality. The extruder is typically composed of a feeding hopper, barrel, screw, die, screw-driving unit and a heating or cooling device. Downstream equipment is used to collect the extrudates for further processing. Monitoring devices on the equipment are a screw-speed controller, an extrusion torque monitor and temperature and pressure gauges. Diagram of a typical extruder is shown in figure1.

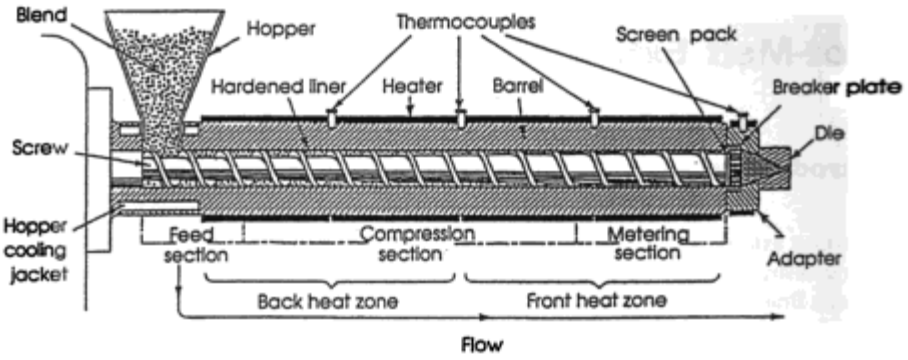

FIG. 1. Schematic diagram of a single screw extruder

During this process, different zones of the barrel are preset to a specific temperature. A blend of the thermoplastic polymers and other processing aids is fed into the barrel of the extruder through the hopper and is transferred by a rotating screw inside the heated barrel. Temperatures of different sections of the barrel are controlled by electrical heating bands and monitored by thermocouples. The materials inside the barrel are heated mainly by the heat

generated due to the shearing action of the rotating screw. The molten mass is eventually pumped into the die, attached to the end of the barrel. The extrudates are subjected to further processing by auxiliary downstream devices.

The functions of the screw are to transfer the material inside the barrel, mix, compress and melt the polymeric materials and pump them through the die. An extruder is generally divided into three zones: feeding section, melting or compression section and metering section as seen in fig1. Types of extruders currently available are single and twin screw extruders. Single screw extruders were used during the early days of this technology. It can be considered as the most basic form of the extruder that simply melts and forms the material. Mixing ability is poor compared to twin screw extruders.., There is a possibility of degradation of material due to heat generation caused by the longer residence time of material. Single screw extruders are an economical option for melt processing but are not ideal for compounding mixtures of plastics with solids or liquids[6]. HME by single screw extruder is a viable method for preparing sustained release wax granules for tablets having low dose of drugs and for tablets prepared with excipient having widely different densities from API[7]. Twin screw extruders were introduced in late 1930s[2]. They provide excellent mixing of the powder materials for melting and forming during this process. Different types of twin screw extruders are available, depending on the manufacturer and for meeting specific market needs. The two main types of twin screw machines are co-rotating and counter rotating which have different screw rotations in the barrels.[6]

MATERIALS IN HME FORMULATIONS

The primary materials in any hot melt extruded formulations are drug, polymers and plasticizers. Other additives can also be added to the formulation such as viscosity inducing agents, anti oxidants, drug release modifiers, bulking agents, swelling agents and lubricants if required. Thickening agents improve the viscosity of formulation and ultimately the plasticity of the solid dosage form. High temperatures needed to process cellulose based polymers may lead to their oxidation. Incorporation of anti-oxidants in formulations containing low molecular weight polymers is recommended. Drug release and dissolution rate of the active compound can be increased or decreased depending on the properties of the rate modifying agent[2].

Polymers: Polymers are the most important excipients in hot melt extruded formulations. They have their characteristic glass transition temperature and melt at temperature little above their Tg. Molten or softened polymers act as binders for granulations, thus requiring no solvents. Mixing occurs thoroughly in the molten state and the drug is embedded in the polymeric matrix. Polymers having Tg below the drug degradation temperatures have been widely utilized as thermal binders and retardants for melt extrusion processing. Some of the polymers which have generally been used in HME include polyvinyl pyrrolidine (PVP), ethyl cellulose(EC), methacrylic acid copolymer, hydroxypropyl methylcellulose (HPMC), hydroxypropyl cellulose (HPC), polyethylene oxide (PEO), eudragit RSPO and eudragit S100, polyethylene glycol (PEG), chitosan, xanthan gum, polyvinyl acetate phthalate (PVAP); HPMC acetate succinate(AS); starch and microcrystalline wax mixtures, cellulose acetate butyrate (CAB), ethyl vinyl acetate (EVAC) and cellulose acetate phthalate(CAP). Some polymers like EC, acrylates, waxes etc. are used for sustained release only and other polymers like PVAP, HPMCAS, and CAP are used for providing delayed release or as alternates to enteric coating. Hydrophilic polymers like HPMC, PEO, HPC, xanthan gum etc. are used to provide sustained release and improve the release depending on the desired purpose.

Plasticizers**:** Plasticizers are important ingredients of HME formulations. They facilitate the process in many ways. They decrease the Tg thereby reducing the processing temperature and ultimately improving the stability of the polymer and the drug. Heat sensitive drugs can be processed at lower temperatures. They decrease the melt viscosity and thus improve the flow in the molten state. They improve the physico-mechanical properties of the final product. They also increase the flexibility of the films used for novel drug delivery systems[8]. The addition of suitable plasticizers can be used to broaden the processing window of any polymer[9] means that gap between melting temperature of the polymer and the degradation temperature of the drug is increased by reducing the Tg of the polymer thereby increasing the efficiency of the process. Some of the plasticizers used in HME are: diethyl phthalate, triacetin, triethyl citrate, acetyl triethyl citrate, acetyl tributyl citrate, propylene glycol, glycerin, dibutyl sebecate, dibutylsorbiton monolaurate, PEG 400 and glycol triacetate. Drugs like Ibuprofen, Ketoprofen, Guaiphenesin and preservatives like methyl paraben reduce the Tg and thus the processing temperature of some

polymers which are generally miscible with them and are therefore termed as nontraditional solid state plasticizers[10-12]. Direct injection of supercritical carbon dioxide can be used as a plasticizer in some formulations and there is no need for additional processing steps as required with other plasticizers.[13,1.5] Supercritical carbon dioxide helps in the preparation of oral monolithic dosage forms with better drug dissolution[14].

APPLICATIONS:

The applications of hot stage extrusion has gained much attention in advanced drug delivery systems due to its potential to manufacture dosage forms with improved physicochemical properties like tablets, capsules, granules, pellets, powders, films, implants, inserts etc[17]. It can provide sustained, modified, targeted and local drug delivery with the use of suitable formulation and process parameters[16]. HME is an efficient technology and is used today for the preparation of solid molecular dispersions with considerable advantages over solvent based processes such as spray drying and coprecipitation[17,] It helps in the scale-up of solid dispersions for solubility enhancements of poorly soluble drugs [16]. This technology is applicable for the topical treatment modalities including recalcitrant disease process and onychomycosis [18]. It can also be used for the development and scale up of drug-in-adhesive type transdermal drug delivery system. The exposure of the materials to humidity and oxygen is avoided during this process, thus minimizing the risk of hydrolysis and oxidation[19]. It is a viable technology to produce thin stable and homogenous drug incorporated polymeric film matrices. These matrices have potential for immediate or sustained release dosage forms, eg. Lidocaine solid solution in the form of films for local delivery [20, 21]. This technique of melt extrusion is used in the fabrication of ocular inserts as solid polymeric rods to be placed in the cul-de-sac of the eyes[22]. Preparation of the enteric capsules by HME is a suitable alternative to film coating for preparing delayed release matrix tablet systems and enteric capsules [23]. This technology is used in the preparation of floating tablets for gastro retentive controlled drug release system and gastro resistant matrix tablets[24]. Taste masked products can also be prepared by choosing the drug and polymer having opposite charges for ionic interaction to take place between them. It is used to prepare tablets for targeted delivery and the controlled release, for eg: 5-amino salicylic acid (ASA) tablets for colonic drug delivery of 5-ASA[25].

Hot melt extruded pellets are unique dosage forms because they can be used for immediate release or controlled release applications depending on the properties of matrix polymers. Conventional pellets must be coated to prevent the rapid drug release even when an insoluble matrix is employed but melt extruded pellets do not require film coating. Extruded pellets can be film coated to further modify the drug release in the GIT[26]**.** Production of minitablets and mini matrices is preferred over the production of pellets, as the scale-up of pelletisation process is a problem. They are generally prepared by using waxes, starch derivatives and matrices. The extrudates are milled and sieved in order to obtain granules, which can be compressed into minitablets. Sustained release mini matrices can also be prepared by HME for obtaining zero order release[27]. Matrix-in-cylinder system consisting of a barrier in the form of hot melt extruded pipes (eg. ethyl cellulose pipe) surrounding a core (HPMC-Gelucire 44/4 core) can be formulated. Drug release characteristics of the matrix-in cylinder system can be modified by changing the length of the system[28].

OPTIMIZATION OF HME PROCESS

Optimization of the melt extrusion process is a must before proceeding for any formulation. Equipment parameters like screw configuration and screw speed; process parameters like temperature, melt viscosity and flow, melt pressure; and formulation parameters like physicochemical properties of the polymer and drug, drug-polymer miscibility and compatibility, glass transition temperature of the polymers, type of plasticizer and the desired drug release from dosage forms have a strong impact on the final product and its performance. Characterization of Physico-mechanical properties of drug and polymers to assess their suitability for this process and the effect of formulation, process and equipment parameters on the product performance must be considered[29].

Formulation parameters: Physico-chemical properties of the powders that affect extrudability are particle size and shape, flow properties, moisture content, particle geometry, bulk density, material compactibility, miscibility of the components and thermal stability. Particle size of polymer influences the release rate of hot melt extruded formulations. Drug release rate is slow in the tablets prepared with the fine particle size fraction of polymer[30]. The mechanical and release properties of hot melt extruded drug loaded films are dependent on the molecular size, weight and moisture of polymer. Optimum moisture content of the extrudates is 2-5% for increasing film's

plasticity without affecting dissolution rate and stability. There is a significant decrease in the tensile strength and Young's modulus and an increase in percentage elongation of the films with increasing moisture content[31]. Free flowing powders are recommended for production by HME.

Drug-polymer compatibility is another important formulation parameter to be considered. Physico-mechanical characterization of the drug and the polymer binary mixtures can provide an insight to the miscibility or immiscibility of the drug and polymer or their interaction and the material behavior during manufacturing. The physico-mechanical properties considered most relevant for melt extrusion process are solubility parameter determination, thermal analysis and rheological analysis. Solubility parameter is a measure of cohesive energy density of the materials. Polymers are generally grouped in two categories based on the difference in the solubility parameter with the drug, miscible polymers and immiscible polymers. Miscible polymers form one phase system that is solid solutions with the drug. Immiscible polymers form a two-phase system, comprising of polymer phase and the drug phase. Compounds with similar solubility parameter values are likely to be miscible, because the energy of mixing released by interactions within the components is balanced by the energy released by interaction between the components. Compounds with solubility parameter difference values less than MPa1/2are likely to be miscible and with such value greater than 10.0MPa1/2 are likely to be immiscible with each other[31]**. A d**rug can exist in different physical states such as the dissolved state or crystalline state depending on its solubility in the polymer. The physical state of drug in the formulation can greatly affect its in vitro and in vivo release characteristics. Knowledge of different states of drug is important to modify its release kinetics.

Thermal analysis by differential scanning calorimetry (DSC) is performed, to predict the miscibility and compatibility of drug and polymer, as a function of polymer concentration and to detect the glass transition temperature of the pure polymer and drug and also Tg of the binary mixture to decide their compatibility and predict the extrusion temperatures. The glass transition temperature (Tg) of a material depends on criteria such as molecular weight, chemical structure, and dimensional structure, cross linking, free volume and intermolecular interactions. DSC of the binary mixture of polymer and drug showing a single Tg indicates the miscibility of the

drug and the polymer and mixture showing two melting isotherms indicates the partial miscibility of the drug in the molten polymer.

Rheological evaluation helps to predict the critical process parameters of HME. Rheological data is useful in assessing drug and polymer miscibility and also in confirming the thermal analysis findings. Effect of shear rate and temperature on viscosity of the mixture and pure polymer are generally studied in this evaluation. A wide range of torque is applied to molten samples and effect of shear rate on viscosity is determined. Zero rate viscosity and energy of activation (Ea) are the parameters determined by this evaluation. Lower zero rate viscosity value of the binary mixture of drug and polymer compared to that of pure polymer melt shows the polymer miscibility with drug since disruption of the polymer structure is indicated. Higher viscosity value indicates immiscibility of the drug in the polymer. Viscosity is found to decrease with increase in the temperatures. The activation energy of the binary mixture required to initiate the flow decreases with both an increase in polymer miscibility and increase in the temperature due to one phase system.

The assessment of the Physico-mechanical properties to HME process is also applied in the estimation of extrusion temperature and motor load. Thermal analysis results particularly Tg and Tm (melting temperature) determination help in the selection of extrusion temperatures for all the barrels except the feeding zone. Extrusion temperature is kept higher than the Tg or Tm of the polymers to ensure the consistent flow of material. Rheological evaluation particularly zero rate viscosity is helpful in estimating the motor load of the HME process[32, 33].

***Formulation development*: Drugs** selected must be stable at the processing temperature and be capable of mixing in the molten state. It should be compatible with the polymer and other excipients used in the process.

Selection of polymer is important and plays a crucial role in the stabilization of hot melt extruded formulations. Polymer choice is a critical factor to obtain the desired drug release profile and has a direct impact on the dissolution profile and API morphology obtained. Processing conditions and attributes of the raw materials should be considered while choosing a polymer for formulation. Processing conditions are selected on the basis of the rheological and thermal properties of the materials to be extruded[34]. Many commercially available, pharmaceutical grade polymers can be used in these formulations.

Polymers selected should not degrade during the process, and must be compatible with the drug. Polymer with a lower Tg is preferred for the processing of heat-labile drugs. Polymers having Tg and melting point below the drug degradation temperature such as PEO, HPC, PVA and polymethacrylates such as eudragit RSPO have been widely used as the thermal binders and retardants for HME processing. The efficiency of melting process depends on the properties of the polymer. The melting process of the polymers of low viscosity and high thermal conductivity is a more efficient process[2].. The desirable attributes of the polymer for amorphous stabilization like solid solution or solid dispersion stabilization are, it should have high Tg, its solubility parameter should be close to that of the API, should have high molecular weight and it should act as moisture scavenger protecting the drug from moisture. Amorphous hydrophilic polymers are often used as components for solid dispersions prepared by melt extrusion. Tg of amorphous polymer is important in hot melt extrusion process because, the drug is incorporated into a rubbery state of amorphous polymer mass. The viscoelastic properties of the polymer namely rubbery or glassy at the manufacturing temperature are affected by the Tg value[35]. Miscible polymers with high Tg are preferred for solubility enhancement by stabilizing the high energy form whereas an immiscible system may be sufficient to produce a controlled release product. Polymers like ethyl cellulose, waxes, xanthan gum, chitosan etc. are used for sustained. and controlled release. Enteric polymers like HPMC acetate succinate are preferred for preparing capsules for delayed release. Combination of polymers or polymer blends can be processed via HME to produce formulations with desired dissolution profiles. The content and viscosity grade of polymers used can be varied to produce the desired release profiles. API crystallinity is also affected by blend composition. Polymer blends with each polymer having one favourable character are preferred instead of single polymer, for eg. combination of HPC and PEO in films[36]. HPC causes increased stability, decreased bioadhesivity and decreased flexibility of PEO films. PEO-causes increased bioadhesivity and mechanical flexibility with decreased stability of HPC films. Polymer blends of HPC and PEO in optimum ratio are preferred for stable HME films with desired physical, mechanical and bioadhesive properties.[37] Minimatrices based on a combination of ethyl cellulose and hydrophilic additive offer a flexible system to tailor the release to the required specification[38]. Drug release from HME tablets

prepared with either chitosan or xanthan gum is pH and buffer species dependent compared to those containing both chitosan and xanthan gum exhibiting pH and buffer species independent sustained release[39].

Selection of Plasticizers is important because they play a significant role in HME formulations. Addition of plasticizers can alter the rate of drug release. Sufficient plasticizer should be incorporated to facilitate extrusion, and produce the desired drug-release profile[34]. Plasticizers can be selected by the pre analytical study by DSC to confirm the polymer-plasticizer compatibility.

Drug Load: The amount of drug that can be loaded depends on, the Ea required to initiate flow, and the torque. Ea should be low for high drug loading. High drug load reduces the polymer content of the matrix resulting in the faster release of the drug.

***Process parameters*:**

Processing parameters like temperature, melt pressure, torque, melt viscosity and residence time must be optimized for each formulation. Processing conditions depend on the chemical stability and physical properties of thermal polymer such as molecular weight, glass transition temperature and melting point (in case of a semi crystalline powder)[2]. Processing conditions are selected on the basis of the rheological and thermal properties of the materials to be extruded. Conditions chosen must generate an acceptable melt viscosity for processing, but they should not result in degradation of any raw materials[34]. Temperature setting is mainly responsible for the melting process and should be set such that there are no problems of degradation of components, viscosity and flow. The processing temperature of an HME process is selected based on the melting or softening temperature of the thermal carrier on the extrusion blend. . The temperature in HME process must be set above the Tg & Tm of the polymers and below the drug degradation temperature. The temperature of the melting section is normally set at 30°c to 60°c above the Tg of amorphous polymer or melting point of semi-crystalline polymers. Plasticizers should be incorporated to reduce the processing temperature. Process temperature should be minimum for facilitating the processing of thermo labile drugs; and it should also control the melt viscosity and facilitate the proper flow of the materials in the molten state. Cooling of the extrudate may result in crystal formation at the surface of the tablet. The addition of hydrophilic polymers to the matrix reduces in the onset and extent of drug recrystallization[42, 34].

Increase in pressure in the compression zone and metering zone should be maintained by the efficient transfer of material. The pressure rise in these zones should be sufficient to provide an efficient output rate of the extrudate. The barrel temperature at the feeding section can be controlled for optimizing the friction at the surface of the barrel because inconsistent material feed may result in a "surge" phenomenon which causes cyclical variations in the output rate, head pressure and product quality[2]. Torque, melt pressure, and drive-motor amperage are indirect measures of melt viscosity. Torque is a measure of the mechanical work needed to move material through an extruder. Melt pressure is the force generated within the extruder as materials are compacted, melted and forced through a die. High viscosity materials result in higher values of torque; melt pressure and drive-motor amperage for a given set of processing conditions because all extrusion equipments have maximum values of these attributes that should not be exceeded. Improper conditions may lead to degradation of the drug and excipients. Processing conditions directly affect the system's melt viscosity because high processing temperature result in lower melt viscosity. Torque in the extruder increases with, increase in viscosity and molecular weight of the material to be extruded, at constant temperature. Torque, barrel pressure and drive-motor amperage can be decreased by incorporating plasticizers in the formulation[34]. Processing conditions and Formulation variables affect the physicochemical properties like porosity and tortuosity, polymer stability and drug release kinetics.

***Equipment Parameters*:**

The equipment parameters generally influencing HME products are screw design, die design, screw configuration and screw speed, etc.

Screw Design: The design of the extrusion screw has a significant effect on the efficiency of HME process. Several parameters are used to define the geometrical features of the screw as given in fig 2.

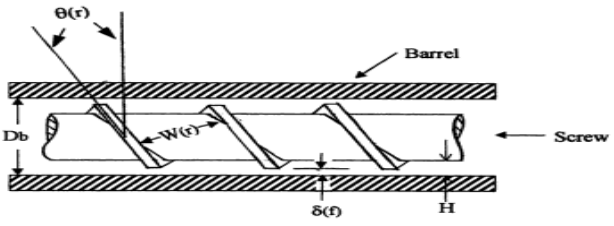

FIG. 2. Geometrical diagram of an extruder screw. Diameter of the barrel (Db) = inside diameter of the barrel; channel depth (H) = distance from screw roots to barrel inner surface; flight clearance ((f) = the distance in between the flight and the barrel inner surface; channel width (Wr)) = distance in between two neighboring flights; helix angle (θr) = angle formed in between the flight and the direction perpendicular to the screw axis.

The purpose of feeding section screw is to compact and transfer the feed stock into the barrel of the machine. Channel depth is normally greatest in this section. Performance of the feeding section depends on the external friction coefficient of feed stock, at the surface of the screw and barrel. Friction at the inner surface of the barrel is the driving force for the material feed, and friction at the surface of screw restricts the forward motion of the material. A high friction coefficient in the barrel and low friction coefficient at the screw surface would contribute to more efficient material transfer in the feed section. The output rate of the extrudate is highly dependent on the channel depth and length of the metering section of the screw which has a shallow channel[2].

Screw configuration: Screw configuration alters the production method as different screw elements like feed rate, metering, mixing and transition discharge can be optimized to suit a particular application. The kneading paddle elements of the screw play an important role in changing the crystallinity and dissolution properties of a solid dispersion prepared via HME. Solid dispersion can be prepared routinely irrespective of the operating condition because the kneading paddle elements can retain the mixture in the machine for a longer period under intense shear. The dissolution profile of kneaded sample shows super saturation, if the kneading paddle elements installed have a twist angle of 60° [40].

Screw speed: Screw revolution speed must be set to maintain the optimum residence time of the materials in the extruder needed for obtaining uniform dispersion of the drug in the polymeric matrix. Degradation may occur due to melt fracture at very high screw speeds. The mechanism of polymer degradation is both thermal and mechanical. Addition of antioxidant reduces the thermal oxidation of polymers like PEO in the solid state[41]. A transparent mass is produced irrespective of the screw revolution speed of kneading paddle elements and an enhanced dissolution profile is obtained. The physico-chemical state of the treated samples is different when the screws consist of feed screw elements alone, without kneading paddle elements. Slow revolution of the screws increases the rate of the drug dissolution[40]

Die Design: The geometrical design of the die controls the physical shape of the molten extrudate. The cross section of the extrudate increases due to swelling as the molten mass leaves the die. The viscoelastic properties of the polymer melt is thus able to recover some of the

deformation imposed by the screw inside the barrel during the extrusion which is also referred to as the "die swelling".

CHARACTERIZATION OF HME FORMULATIONS

Evaluation of HME products is important to assess the product performance. The release profile from melt extruded sustained, controlled, targeted and delayed release formulations are studied by carrying out dissolution. The surface morphology (crystallinity, amorphous nature,) of drug is examined by scanning electron microscopy (SEM). HME formulations provide direct evidence of the presence of dispersed drug within the matrix. X-ray Powder diffraction is used to assess the crystallinity. Patterns of high intensity reveal crystallinity. Hot melt extruded formulations are also evaluated by hydration and erosion studies, thermal behavior analysis by DSC, modulated differential scanning calorimetry (MDSC), FT-IR and stability studies.

Evaluation of hot melt extruded films includes other specific tests like moisture sorption studies, bio-adhesion studies, Young's modulus determination, % elongation and tensile strength Stability testing of the films is done according to the ICH guidelines.

CONCLUSION

HME technology is an advanced technique for the manufacture of different conventional dosage forms and novel drug delivery systems. Desired release profiles can be obtained by using suitable polymers for controlled and sustained release dosage forms. Good content uniformity is obtained for dosage forms prepared by HME. Bio-availability of the poorly-soluble drugs can be improved by modifying their release profiles. Proper optimization of the process is essential for the assurance of product quality and performance.

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Corresponding Author:

Sadhna khatry*[1]

Sadhna khatry, Director,

Dev Bhoomi Institute of Pharmacy and Research,

Manduwala, Dehradun, Uttarakhand.

Email: *sadhna_khatry@yahoo.com*