Review Article

HOT-MELT EXTRUSION

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ABSTRACT

Hot-melt extrusion (HME) is one of the most widely applied processing technologies in the plastic, rubber and food industry. Interest in the pharmaceutical applications is growing rapidly and is evident from the increasing number of patents and publications. Limitations related to bioavailability and site specific drug delivery can be overcome by this technique. This technology has gained focus because of its ease of operation and fast processing. Melt extrusion is considered to be an efficient technology with particular advantages over solvent processes like co-precipitation for the manufacture of a variety of dosage forms and formulations such as granules, pellets, tablets, suppositories, implants, stents, transdermal systems and ophthalmic inserts. 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 zones: feeding zone, melting zone, and the metering zone. HME also includes of its advantages, applications of hot melt extrusion technology and the optimization of HME process through which product quality and performance is assured.

Keywords: Hot melt extrusion, pellets, implants, stents, extruders.

INTRODUCTION

The word 'extrusion' is derived from the Latin 'extrudere', which literally means to press out or to drive out. A recent FDA guideline (FDA Pharmaceutical cGMP for the 21st Century, 2004) for the enhancement and modernization of the pharmaceutical industry has facilitated the move towards continuous manufacturing. In addition to being a proven manufacturing process, continuous extrusion meets the goal of the US Food and Drug Administration's process analytical technology (PAT) initiative for designing, analysing, and controlling the manufacturing process through quality control measurements during processing. These are achievable with HME technology.

Interest in HME techniques for pharmaceutical applications is growing rapidly with well over 100 papers published in the scientific literature in the last 12 years. Also, the number and percentage of HME patents issued for pharmaceutical systems has steadily increased since the early 1980's with international scope shown in figure 1 and 2[1-4].

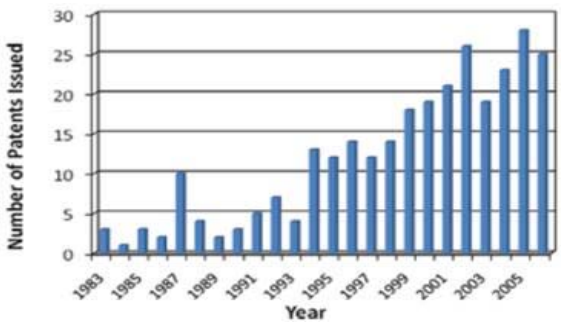

Figure 1: The number of hot-melt extrusion patents issued for pharmaceutical applications from 1983 to 2006

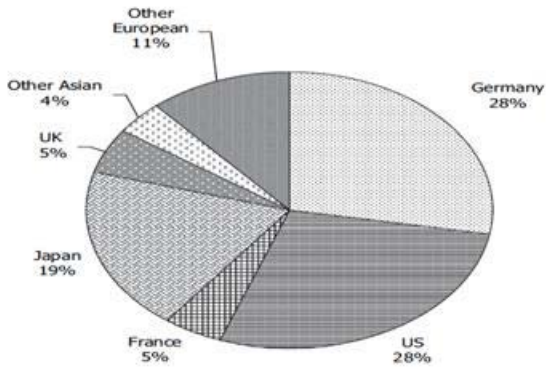

Figure 2: The number and percentage of hot-melt extrusion patents issued by country since 1983 for pharmaceutical application

Definition

Hot Melt Extrusion can be simply defined as the process of forming a new material (extrude) by forcing a raw material or blend (API and Excipient) with a rotating screw through a die or orifice under set conditions such as temperature, pressure, rate of mixing and feed-rate, for the purpose of producing a stable product of uniform shape and density.

Objectives

- To increase the drug's dissolution rate and bioavailability
- To control or modulate drug release
- To mask the drug's taste
- To stabilize the API
- To create parenteral depots and topical drug delivery systems

Advantages

HME offers several advantages over traditional pharmaceutical processing techniques including in table 1.

Table 1: Advantages of HME over traditional pharmaceutical processing techniques

Feature	Benefits
Solvents not required	Environmentally friendly, economical; No residual solvent in final product; It avoids the degradation problems there by resulting in improved stability.
Fast and a continuous operation.	Reduced production time, fewer processing steps; Efficient scale-up from laboratory to large scale production.
Excellent mixing and agitation achieved	Improved content uniformity (99%-101%)
Compressibility not required	Useful for powders with low compressibility index; Poorly compactable materials can be easily formulated into tablets.
Polymer serve multipurpose	Less number of excipients required; cost effective.
Greater thermodynamic stability than that produced by other melt methods.	Fewer tendencies towards recrystallization.
Closed process unit	Prevent cross contamination.
Possibility of online analytics	Process control.
High out-puts	On commercial scale >500 kg/hr are possible.
Medium to high load of API	>50% is possible with this technique
Minimum residence time and short thermal exposure of the active pharmaceutical ingredients (API)	Allows the processing of thermo labile drugs.
Best processing technique	Extruded solid solutions offer higher thermodynamic stability than those prepared by alternative processes, such as spray drying, solvent evaporation, and other hot-melt methods.

Other

- Clinically advantaged dosage forms, such as drug abuse and dose dumping deterrent technology.
- Production of a wide range of performance dosage forms
- Less labours and equipment demand.

Disadvantages

- Thermal process (drug/polymer stability)
- Flow properties of the polymer are essential to processing.
- Limited number of available polymer
- Requires high energy input.
- Lower-melting-point binder risks situations where melting or softening of the binder occurs during handling and storage of the agglomerates.
- Higher-melting-point binders require high melting temperatures and can contribute to instability problems especially for heat-labile materials such as proteins, peptides, etc.
- Non-traditional equipment and requires education and training[2, 3, 5, 6].

MATERIALS USED IN HME FORMULATIONS

The materials used in the production of hot melt extruded dosage forms must meet the same level of purity, safety and some degree of thermal stability in addition to acceptable physical and chemical stability. The thermal stability of each individual compound and of the composite mixture should be sufficient to withstand the production process**.**

Active Ingredient

Active ingredients 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.

Table 2: Drugs that can be processed by Hot-melt extrusion techniques

Drug	*Tm* (°C)
Nifedipine	175
Indomethacin	162.7
Piroxicam	204.9
Tolbutamide	128.
Lacidipine	184.8
Theophylline	255
17β-estradiol hemihydrate	_
Oxprenolol hydrochloride	108
Fenoprofen calcium	–
Lidocaine	68.5
Phenylpropanolamine Hydrochloride	192
Hydrochlorothiazide	274
Carbamazepine	192
5-Aminosalicylic acid	280
Diltiazem Hydrochloride	210
Ketoconazole	148–152
Guaifenesin	78.5
Ketoprofen	94

2.2 Polymers

Molten or softened polymers act as binders for granulations, thus no requiring 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.

The selection of polymer for hot-melt extrusion process mainly depends on drug–polymer miscibility, polymer stability and function of final dosage form. A variety of carrier systems have been studied or used in hot-melt

extrusion dosage forms. Some of the polymers which have generally been used in HME include in table 3 and 4.

Table 3: Hydrophilic meltable polymers

Hydrophilic Meltable Binder	Typical Melting Range (°C)
Gelucire 50/13	44 - 50
Poloxamer 188	50.9
Polyethylene glycol	
2000	42–53
3000	48–63
6000	49–63
8000	54–63
10000	57–64
20000	53–66
Stearate 6000 WL1644	46–58

Table 4: Hydrophobic meltable binders

Hydrophobic Meltable Binder	Typical Melting Range (°C)
Beeswax	56–60
Carnauba wax	75–83
Cetyl palmitate	47–50
Glyceryl behenate	67–75
Glyceryl monostearate	47–63
Glyceryl palmitostearate	48–57
Glyceryl stearate	54–63
Hydrogenated castor oil	62–86
Microcrystalline wax	58–72
Paraffin wax	47–65
Stearic acid	46–69
Stearic alcohol	56–60

Plasticizers

Plasticizers decrease the Tg thereby reducing the processing temperature and ultimately improving the stability of the polymer and the drug. They improve the physico-mechanical properties of the final product and also increase the flexibility of the films used for novel drug delivery systems.

Table 5: Common plasticizers used in pharmaceutical dosage forms

Type	Examples
Citrate esters	Triethyl citrate, tributyl citrate, acetyl triethyl citrate, acetyl tributyl citrate
Fatty acid esters	Butyl stearate, glycerol monostearate, stearyl alcohol
Sebacate esters	Dibutyl sebacate
Phthalate esters	Diethyl phthalate, dibutyl phthalate, dioctyl phosphate
Glycol derivatives	Polyethylene glycol, propylene glycol
Others	triacetin, mineral oil, castor oil
Vitamin E TPGS	D-α-tocopheryl polyethylene glycol 1000 succinate

Other processing Aids

The excessive temperatures needed to process unplasticized or under plasticized polymers may lead to polymer degradation. The stability of polymers that are susceptible to degradation can be improved with the addition of antioxidants, acid receptors and or light absorbers during hot melt extrusion. Other materials have been used to facilitate hot-melt extrusion processing. Waxy materials like glyceryl monostearate have been reported to function as a thermal lubricant during hot-melt processing. Vitamin E TPGS has been reported as to plasticise polymers and enhance drug absorption[1, 2, and 4].

HME EQUIPMENT

Typical pilot plant extruders have diameters ranging 18–30 mm, whereas production machines are much larger with diameters typically exceeding 50 mm. In the pharmaceutical field, hot melt extrusion equipment consists of an extruder, downstream auxiliary equipment for extruder and other monitoring tools used for performance and product quality evaluation.

Individual components within the extruder are

- Feed hopper
- A temperature controlled barrel
- Rotating screws
- Screw-driving unit
- Die

Feed hopper

It is used to feed the material into the feed zone of barrel.

Barrel

The extruder barrel is a heavy steel cylinder that houses the screw of extruder. The barrel is made of highly wear-resistant materials. The inner surface of the barrel is reinforced with an iron-nitriding or bimetallic alloying technique. The barrel is often manufactured in sections, which are bolted or clamped together. Barrel sections are heated by electric heaters or liquid. Barrel-cooling facilitates a temperature set point to maintain desired melt viscosity within the process section. Extruder barrels are typically cooled by liquid and sometimes air. The most effective heat transfer design uses axial cooling bores inside the barrel and close to the process melt stream. The temperature of all the barrels are independent and can be accurately controlled from low temperatures (30^0C) to high temperatures (300^0C) degradation by heat can be minimized.

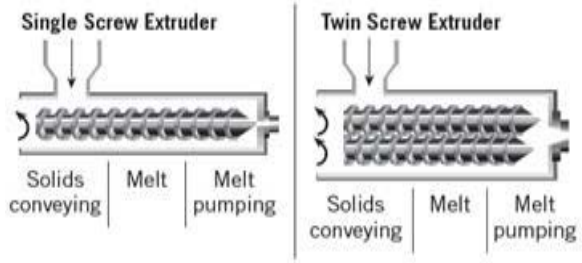

Figure 3: Cross-section of single and twin screw extruder barrel.

Rotating screws

Generally, the extruder consists of one or two rotating screw inside a stationary cylindrical barrel. It is common for the extrusion screw to be characterized by the" length to diameter ratio" or L/D. This term expresses the length of the screw divided by the diameter. For instance, an extruder 1000 mm long with a 25 mm screw diameter has a 40:1 L/D. Typical extrusion process length are in the 20 to 40:1 L/D range or longer.

Die

An end-plate die, connected to the end of the barrel, determines the shape of the extruded product.

Screw-driving unit

The extrusion drive system generally comprises motor, gearbox, linkage and thrust bearings.

Auxiliary downstream equipment

Downstream equipment for cooling, cutting and collecting the finished product

Monitoring devices on the equipment include

- Temperatures are normally controlled by electrical heating bands and monitored by thermocouples/ temperature gauges
- A screw speed-controller
- An extrusion torque monitor
- And pressure gauges.

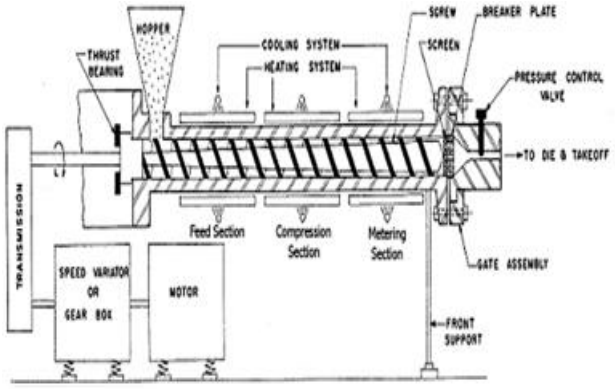

Figure 4: Schematic diagram of a single screw extruder

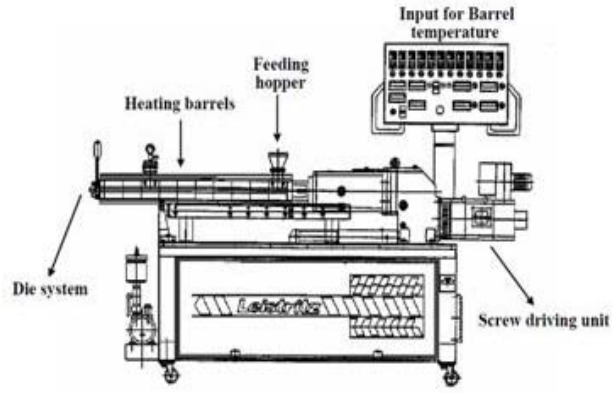

Figure 5: Micro-18 Twin screw co-rotating Leistritz extruder

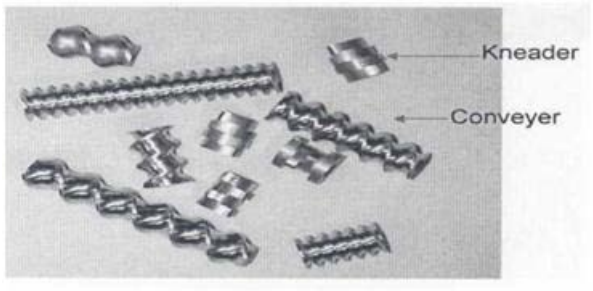

Figure 6: Screw and kneading elements

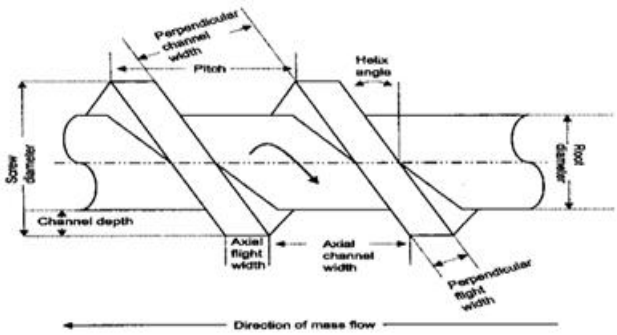

Figure 7: Extrusion screw geometry

There are two types of screw extruders are mainly Single and Twin screw extruders.

Single screw-extrusion

Single screw extruders were used during the early days of this technology. This is a fundamental operation for polymer processing and used to increase pressure within a polymer melt, allowing extrusion through a die or injection into a mould. Although a relatively simple process, single screw extrusion does not possess the mixing capability of a twin-screw machine and is, therefore, not the preferred approach for the production of pharmaceutical formulations. Single screw extruders are an economical option for melt processing but are not ideal for compounding mixtures of plastics with solids or liquids.

Advantages of single-screw compared to twin-screw extruders

- Mechanical simplicity
- Low cost of investment.

Disadvantages

- 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.

Twin screw extrusion

Twin screw extruders were introduced in late 1930s. They provide excellent mixing of the powder materials for melting and forming during this process. Twin screw extruders can process as little as a 20g batch and more than 500kg/hr.

Industrially, twin-screw extrusion has become extremely favourable because of process practicality and the ability to combine separate batch operations into a single continuous process, thus increasing manufacturing efficiency. Different types of twin screw extruders are available, depending on the manufacturer and for meeting specific market needs.

There are two families of twin screw extruders: high-speed energy input (HSEI) twin-screw extruders, which are primarily used for compounding, reactive processing and/or de-volatilization, and low-speed late fusion (LSLF) twin-screw extruders, designed to mix at low shear and pump at uniform pressures.

Twin- screw extruders, as the name implies, use two screws usually arranged side by side. The two main types of twin screw machines can either rotate in the same (co-rotation) or the opposite direction (counter/contra-rotation).

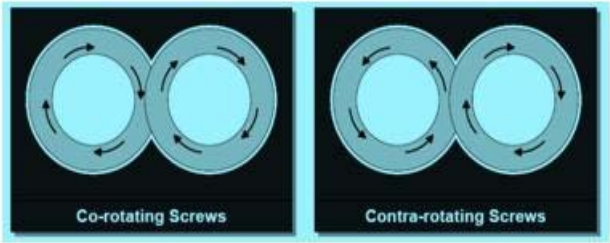

Figure 8: Co-rotating and counter-rotating twin screw extruder

The counter-rotating designs are utilized when very high shear regions are needed as they subject materials to very high shear forces as the material is squeezed through the gap between the two screws as they come together. Generally, counter-rotating twin-screw extruders suffer from disadvantages of potential air entrapment, high-pressure generation and low maximum screw speeds and output.

The co-rotating and counter-rotating twin screw extruders can be further classified as either intermeshing or non-intermeshing. In most cases co-rotating intermeshing twin screw extruders are being preferred because the greater degree of conveying achievable and the shorter residence times, high screw speed, high output. This design itself is self-wiping, where it minimizes the non-motion and prevents localized overheating of materials within the extruder. The extruder operates by a first in/first out principle since the material does not rotate along with the screw.

Non-intermeshing extruders, on the other hand, are often used for processing when large amounts of volatiles need to be removed and when processing highly viscous materials. Non-intermeshing extruders allow large volume de-volatilisation via a vent opening since the screws are positioned apart from one another. Non-intermeshing extruders are not susceptible to high torques generated while processing highly viscous materials for the same reasons.

The twin-screw extruder is characterized by the following descriptive features

- **Short residence time:** ranges from 5-10 min depending on the feed rate and screw speed.
- **Self-wiping screw profile:** ensures near complete emptying of the equipment and minimizes product wastage on shutdown.
- **Minimum inventory:** Continuous operation of the equipment coupled with the continuous feeding of the material helps in reducing inventories of work in progress.
- **Versatility:** Operating parameters can be changed easily and continuously to change extrusion rate or mixing action. The segmented screw elements allow agitator designs to be easily optimized to suit a particular application. Die plates can also be easily exchanged to alter the extrudate diameter. This allows processing of many different formulations on a single machine, leading to good equipment utilization.
- **Superior mixing:** The screws have various mixing elements which impart two types of mixing. In the distributive mixing, the materials are uniformly blended but not broken down and implemented for mixing heat and shear-sensitive APIs with minimal degradation. In dispersive mixing ideally breaks droplet or solid domains to fine morphologies using energy at or slightly above the threshold level needed. This mixing aids in efficient compounding of two or more materials in the twin-screw extruder.

Advantages of twin-screw compared to single-screw extruders

- Easier material feeding
- High kneading potential
- High dispersing capacities
- Less tendency to overheat (important for sensitive API)
- Provides more stable melting process, shorter residence time & greater output[1, 2, 5, 8, 9].

HME PROCESS

The theoretical approach to understanding the melt extrusion process is therefore, generally presented by dividing the process of flow into four sections:

Feeding of the extruder.

Conveying of mass (mixing and reduction of particle size).

Flow through the die.

Exit from the die and down-stream processing.

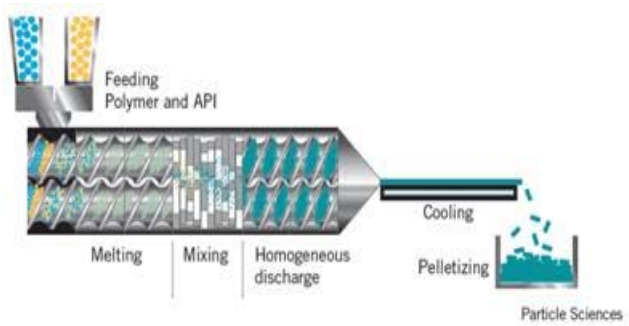

Figure 9: Hot melt extrusion process

Feeding of the extruder

The purpose of the feeding section is to compact and to transfer the feed stock into the barrel of the machine through the hopper. Mass flow feeders are used in conjunction with extruders to accurately meter solids. Gravimetric feeding is typically specified for GMP installations.

Conveying of mass

Based on the geometrical design and function of the rotating screw inside a stationary barrel that may be conventionally subdivided into three distinct zones: feed zone, compression zone and metering zone-

The depth and/or pitch of the screw flights differ within each zone, generating variable pressure along the screw length (zone dependent). The channel depth is normally greatest in feed zone. Because of the large screw flight depth and pitch, the pressure within the feed zone is very low, allowing for consistent feeding from the hopper and gentle mixing of API and excipients.

The primary function of the subsequent compression zone is to melt, homogenize and compress the extrudate so that it reaches the metering zone in a form suitable for extrusion. Consequently, the compression zone must impart a high degree of mixing and compression to the material. This is achieved by decreasing the screw pitch and/or the flight depth, resulting in a gradual increase in pressure along the length of the compression zone.

The final section, the metering zone stabilizes the pulsating flow of the matrix, thus ensuring the extruded product has a uniform thickness. Constant screw flight depth and pitch helps maintain continuous high pressure to ensure a uniform delivery rate of molten material through the extrusion die and hence a uniform product.

Flows through the die

The molten mass is eventually pumped into the die, attached to the end of the barrel. The geometrical design of the die will control the physical shape and size of the molten extrudate. Different types of exit dies are used to shape the extrudate to the desired profile. These dies include sheet and film dies used in transdermal film applications, strand dies used for medical tubing and some drug-eluting devices, shape dies used in blow moulding, and co-extrusion dies used in reservoir device designs.

Exit from the die and Downstream Processing

Downstream extrusion equipment used to finish, shape and analyze the extruded product. After leaving the die in the form of continuous strands or ribbons, cooling and cutting is performed, resulting in required particle size. Process Analytical Technology (PAT) instruments such as in line NIR (Near Infrared Spectroscopy) can be used to check the homogeneity of the active ingredient in the extrudate.

Different downstream auxiliary components are also used in the finishing process, including:

- **Conveyor belts**: for moving the extruded product from the die to the end of the line. Water baths, air knives, nitrogen for cooling the extrudate on stainless steel conveyor.
- **Chill rolls**: for cooling the molten strands or ribbons.
- **Strand-cutters**: for cutting the extrudate into tubing or rods
- **Pelletizers:** for cutting the extrudate into smaller pieces (typically between 0.5 and 5mm) for direct capsule filling and in-line spheronisation is also possible.
- **Die-face palletisation** is also common, where the pellets are cut at the die face and conveyed/cooled by various methods, including chilled air chimneys and vibratory towers.
- **Flakers:** used to chop the film to required sizes.
- **Calender**: used for direct shaping.
- **Film and lamination systems:** for transmucosal and transdermal applications. Film thickness can be adjusted by changing the die opening, the mass flow rate introduced into the extruder, screw speed, the rotation speed of the chill rolls, or the torque winder.
- **Spoolers**: for extrudate collection[1, 2, 4, 7, 9-11].

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[1].

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.
- It can provide sustained, modified, targeted and local drug delivery with the use of suitable formulation and process parameters**.**
- 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 co-precipitation. It helps in the scale-up of solid dispersions for solubility enhancements of poorly soluble drugs.
- It can also be used for the development and scale up of drug-in-adhesive type transdermal drug delivery system.
- 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, e.g. Lidocaine solid solution in the form of films for local delivery**.**
- 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.
- Preparation of the enteric capsules by HME is a suitable alternative to film coating for preparing delayed release matrix tablet systems and enteric capsules.
- This technology is used in the preparation of floating tablets for gastro retentive controlled drug release system and gastro resistant matrix tablets.
- 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 e.g.5-amino salicylic acid (ASA) tablets for colonic drug delivery of 5-ASA**.**
- 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.
- 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.
- Matrix-in-cylinder system consisting of a barrier in the form of hot melt extruded pipes (e.g. 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[1, 2, 11].

RESEARCH DEVELOPMENTS

More recent scientific articles have described the use of HME for the manufacture of solid dispersions and for the development of Minimatrices.

De Brabander *et al.* (2000) described the preparation of matrix mini-tablets that minimize the risk of dose dumping, reduce inter and intra-subject variability and provide highly dispersive formulations within the gastrointestinal tract. This was complemented by further investigations into the properties of sustained release mini-matrices manufactured from ethyl cellulose, HPMC.

Chokshi *et al.* (2005) stable, amorphous indomethacin dispersions have been manufactured using pharmaceutically acceptable hydrophilic polymers.

HME floating tablets have been examined by Fukuda *et al.* (2006) studied additionally, targeted drug delivery systems, including enteric matrix tablets and capsules systems, have been extruded.

Miller *et al.* (2007) they have demonstrated the ability of HME to act as an efficient dispersive process for aggregated, fine engineering particles to enhance their wettability and improve dissolution rate properties.

J.P. Remon *et al*. (Oct 2009) studied the different types of ethyl cellulose-based mini-matrices were prepared by hot-melt extrusion and thoroughly characterized in vitro. Metoprolol tartrate was used as model drug, and various amounts and types of polyethylene glycol (PEG)/polyethylene oxide (PEO) were added as release rate modifiers.

Mcginity James *et a*l. (Feb 2010) described **b**riefly, a bioavailable sustained release oral opioid analgesic dosage form is described comprising a plurality of multiparticulates produced via melt extrusion techniques.

Meredith Clark *et al*. (Oct 2011) studied the microbicide intravaginal rings (IVRs) are a promising woman-controlled strategy for preventing sexual transmission of human immunodeficiency virus (HIV). An IVR was prepared and developed from polyether urethane (PU) elastomers for the sustained delivery of UC781 (used as an anti-HIV microbicide), a highly potent nonnucleoside reverse transcriptase inhibitor of HIV-1. PU IVRs

containing UC781 were fabricated using a hot-melt extrusion process.

Markus *et al*. (Dec 2011) Studied the Darunavir (TMC 114) is a protease inhibitor used in the therapy of HIV-1. The aim of this study was to formulate 800mg of Darunavir in a single unit dosage form, with suitable mechanical properties and dissolution behaviour, using a corrugating twin screw extruder[12-18].

MARKETED PRODUCTS

The interest in HME is growing rapidly. The US and Germany hold approximately more than half (56%) of all issued patents. In spite of this increased interest, there are few commercialized HME pharmaceutical products currently marketed shown in table 6[1, 18].

Table 6: Approved pharmaceutical products that utilize HME

Product	Company
Lacrisert (HPC Rod)	Merck
Zoladex (Goserelin Acetate Implant)	AstraZeneca
Implanon (Etonogestrel)	Organon
Gris-PEG (Griseofulvin)	Pedinol Pharmacal
Rezulin (Troglitazone)	Wyeth
Palladone (Hydromorphone)	Purdue Pharma
NuvaRing (Etonogestrel, Ethinyl Estradiol)	Merck
Norvir (Ritonavir)	Abbott Laboratories
Kaletra (Ritonavir/Lopinavir)	Abbott Laboratories
Eucreas (Vildagliptin/Metformin HCL)	Novartis
Zithromax (Azythromycin)	Pfizer
Orzurdex (Dexamethasone)	Allergan

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. Bioavailability of the poorly-soluble drugs can be improved by modifying their release profiles. The design of screw assemblies and extruder dies are two major areas, which have significant impact on product quality and degradation of drug and polymers. Drugs which are sensitive to elevated temperatures can be processed successfully when the residence time is short. Proper optimization of the process is essential for the assurance of product quality and performance.

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