A REVIEW ON PARENTERAL DRUG DELIVERY SYSTEM

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ABSTRACT

Parenteral formulations, particularly intravascular ones, offer a unique opportunity for direct access to the bloodstream and rapid onset of drug action as well as targeting to specific organ and tissue sites. Parenteral preparation have been traditionally used to accomplish these tasks and there are several products on the market using these injectable & control release novel drug & implant formulations. The broader application of these novel control drug delivery systems in parenteral drug delivery, however, particularly with new chemical entities, has been limited due primarily to the following reasons: a) only a small number of parenteral drug excipients are approved, b) there is increasing number of drugs that are partially or not soluble in conventional oils and other lipid solvents, and c) the ongoing requirement for site-specific targeting and controlled drug release. Thus, there is growing need to expand the array of targetable control drug delivery & drug implant systems to deliver a wide variety of drugs and produce stable formulations which can be easily manufactured in a sterile form, are cost effective and at least as safe and efficacious as the earlier developed systems. These advanced parenteral implant-based systems are at various stages of preclinical and clinical development which include nanoemulsions, nanosuspensions, liposomes, niosomes, nano partical, micro partical,pro- drug and needal free injection. This review article will showcase these injectable controlled release systems, advanced parenteral drug delivery system,implant&novel technologies in implant, recent innovations in sterile drug delivery devices and discuss advances in relation to formulation development, processing and manufacturing, and stability assessment.

INTRODUCTION

Parenteral dosage forms differ from all other drug dosage forms, because they are injected directly into body tissue through the primary protective systems of the human body, the skin, and mucous membranes. They must be exceptionally pure and free from physical, chemical, and biological contaminants. These requirements place a heavy responsibility on the pharmaceutical industry to practice current good manufacturing practices (cGMPs) in the manufacture of parenteral dosage forms and on pharmacists and other health care professionals to practice good aseptic practices (GAPs) in dispensing parenteral dosage forms for administration to patients. Certain pharmaceutical agents, particularly peptides, proteins, and many chemotherapeutic agents, can only be given parenterally, because they are inactivated in the gastrointestinal tract when given by mouth. Parenterally-administered drugs are relatively unstable and generally highly potent drugs that require strict control of administration to the patient. Due to the advent of biotechnology, parenteral products have grown in number and usage around the world. Parenteral preparations may require the use of excipients, for example:

- To make the preparation isotonic with respect to blood,
- To adjust the pH, to increase solubility,
- To prevent deterioration of the active substances or
- To provide adequate antimicrobial properties, but not to adversely affect the intended medicinal action of the preparation or, at the concentrations used, to cause toxicity or undue local irritation.

Several categories of parenteral preparations may be distinguished:
1. Injections
2. Infusions
3. Implants
4. Concentrates for injections or infusions
5. Powders for injections or infusions
6. Gels for injections

ADVANTAGES

1. An immediate physiological response can be achieved if necessary, which can be of prime consideration in clinical condition such as cardiac arrest, asthama and shock.
2. Parenteral therapy is required for drugs that are not effective orally or that are destroyed by digestive secretions such as insulin other hormones and antibiotics.
3. Drug for uncooperative, nauseous or unconscious patients must be administered by injection.
4. When desirable, parenteral therapy gives the physician control of the drug since the patient must return for continued treatment, also in some cases the patient cannot be relied upon to take oral administration.
5. Parenteral administration can results in local effect for drugs when desired, as in dentistry and anesthesiology.
6. In case in which prolonged drug action is wanted, parenteral Forms are available, including the long intrartially and the long acting penecillins administered deep intra muscularly.
7. Parenteral therapy provides the means of correcting serious disturbances of fluid and electronic balances.
8. When food cannot be taken by mouth, total nutritional requirement can be supplied by the parenteral route.

DISADVANTAGE

1. The dosage form must be administered by trained personnel and require more time than those administered by other routes.
2. Parenteral administration requires strict adherence to aseptic procedures, and some pain on injection is inevitable.
3. It is difficult to reverse its physiological effect.
4. The manufacturing and packaging requirements, parenteral dosage forms are more expensive than preparations of given by other routes. [1, 2]

INJECTABLE DRUG DELIVERY

Injections are sterile solutions, emulsions or suspensions. They are prepared by dissolving, emulsifying or suspending the active substance(s) and any added excipients in water, in a suitable non-aqueous liquid, that may be non-sterile where justified, or in a mixture of these vehicles.

APPROACHES

Several pharmaceutical formulation approaches may be applied to the development of parental controlled release or sustained release formulations. The most commonly used techniques are as follows.
1) Use of viscous, water miscible vehicles such as an aqueous solution of gelatin or poly vinyl pyrrolidine.
2) Use of water immiscible vehicles such as vegetable oil plus water repelling agent such as aluminium mono stearate.
3) Formation of thixotropic suspensions
4) Preparation of water insoluble drug derivatives such as salts, complexes and esters
5) Dispersion in polymeric micro spheres or microcapsules such as lactide glycolide homopolymer or copolymers.
6) Coadministration of vaso constrictors.
7)These techniques may be used alone for example formation of aqueous insulin zinc suspension or in combination for example penicillin G procaine suspension in vegetable oil gelled with aluminium monostearate.[3,4,5]
INJECTABLE CONTROLLED RELEASE FORMULATION

The injectable depot formulation was developed with the primary objective of simulating the continuous drug administration of IV infusion. It often results in reduced drug dose, decreased side effects, enhanced patient compliance and improved drug utilization.

Reasons for development of PDS (Parenteral Depot System)
1. No surgical removal of depleted system is required as it is metabolized in non toxicological by product.
2. The drug release from this system can be controlled by following: Diffusion of drug through the polymer, Erosion of the polymer surface with concomitant release of physically entrapped drug, Cleavage of covalent bond between the polymer bulks or at the surface followed by diffusional drug loss, Diffusion controlled release at the physically entrapped drug with bio adsorption of the polymer until drug depletion. Depot formulation may be classified on the basis of the process used for controlled drug release as follows:

DISSOLUTION CONTROLLED DEPOT FORMULATION

In this depot formulation the rate of absorption is controlled by the slow dissolution of drug particles in the tissue fluid surrounding the formulation or in the formulation.

(Q/t) d under sink condition is defined by :

(Q/t) d = sa ds cs/hd

Where sa = surface area of the drug particles in contact with the medium

ds= is the diffusion coefficient of drug molecules in the medium

Cs= is the saturation solubility of the drug in the medium.

Hd = thickness of the hydrodynamic diffusion layer surrounding each drug particle.

Basically two approaches can be utilized to control the dissolution of drug particle to prolong the absorption and hence the therapeutic activity of the drug.[6]

Formation of salt or complexes with low aqueous solubility
Examples of dissolution controlled depot formulation using salt formation technique are:

— Penicillin G procaine (cs = 4 mg / ml) and penicillin G benzathine (cs=0.2 mg /ml)

— Naloxone pamoate and naltrexone Zn tannate from water soluble hydrochloride salts of naloxone and naltrexone respectively

Both aqueous suspension as well as oleaginous suspension of penicillin G procaine and penicillinG benzathine produces prolonged therapeutic activities. Penicillin benzathine and penicillin G procaine combination as well as oleaginous suspension of naloxone pamoate and naltrexone Zn tannate in vegetable oil all produce prolonged therapeutic activities.[7,8]

Aqueous Suspension

Suspension of macro crystals large crystals are known to dissolve more slowly than small crystals this is called macro crystal principle and can be applied to control the rate of drug dissolution e.g.: aqueous suspension of testosterone isobutyrate for I.M injection in contrast with the suspension in plain peanut oil i.e. without gelation with aluminium monostearate or with aqueous suspension this macrocrystal principle was followed fairly well. Several years following the development of depot penicillin oleaginous suspension, it was discovered that the therapeutic serum concentration of penicillin can be substantially prolonged by formulating penicillin G procaine in an aqueous thixotropic suspension. This was accomplished by maintaining a high solid vehicle ratio (40%to 70% of milled and micronized penicillin G procaine particles) Its prolonged action is partly because these thixotropic suspensions tend to form compact and cohesive depots at the site of intramuscular injection. Leading to the slow release of penicillin G procaine and partly because of the low aqueous solubility of the procaine salt of penicillin G that renders the intramuscular absorption of penicillin under the control dissolution of penicillin G procaine in the tissue fluid.[9]

ADSORPTION TYPE DEPOT FORMULATION

This type of depot preparation is formed by the binding of drug molecule to adsorbents in this only the unbound , free species of the drug is available for absorption as soon as the unbound drug molecules are absorbed a fraction of the bound drug molecule is released to maintain equilibrium.

E.g. vaccine preparations in which the antigens are bound to highly dispersed aluminium hydroxide gel to sustain their release and hence prolong the duration of stimulation of antibody formation. Prolongation of insulin activity was made by complexing insulin with protamine. Protamine-insulin complex releases upto 24 hrs on subcutaneous injection. Protamine –Zn – insulin complex when given subcutaneous releases upto 36 hrs but it has slow onset of action 4 to 8 hrs.

Others: Insulin-Zn-Protein complexes like:

a) Isophane insulin suspension (USP) has rapid onset of action (1-1.5 hrs) and moderate duration of activity (24 hrs).

b) Gliobin-Zn-insulin injection USP, onset of action and release pattern similar to Isophane.
ENCAPSULATION TYPE DEPOT FORMULATIONS

This type of depot formulation is prepared by encapsulating drug solids within a permeation barrier or dispersing drug particles in a diffusion matrix. Both permeation barrier and diffusion matrix are fabricated from biodegradable or bioabsorbable macromolecules such as gelatin, dextran, polylactate, lactide glycolide co polymers phospholipids and long chain fatty acids and glycerides.

E.g: Naltrexone palmoate releasing biodegradable micro capsules, the release of drug molecules is controlled by the rate of permeation across the permeation barrier and the rate of biodegradation of the barrier macromolecules.

ESTERIFICATION TYPE DEPOT FORMULATION:

This depot preparation is produced by esterifying a drug to form bioconvertable pro drug type ester and then formulating it in a inject able formulation this formulation forms a drug reservoir at the site of injection. Eg. fluphenazine enanthate testosterone 17 cypionate in oleagenous solution.[10]

IMPLANTS

An implant is a medical device manufactured to replace a missing biological structure, support a damaged biological structure, or enhance an existing biological structure. Medical implants are man-made devices, in contrast to a transplant, which is a transplanted biomedical tissue. The surface of implants that contact the body might be made of a biomedical material such as titanium, silicone or apatite depending on what is the most functional. In some cases implants contain electronics e.g. artificial pacemaker and cochlear implants. Some implants are bioactive, such as subcutaneous drug delivery devices in the form of implantable pills or drug-eluting stents. Implants are sterile, solid preparations of a size and shape suitable for parenteral implantation and release of the active substance(s) over an extended period of time. These are made by compression, melting or sintering. They generally consist of the drug and the rate controlling excipients.

APPROACHES TO THE DEVELOPMENT OF IMPLANTABLE DRUG DELIVERY SYSTEM

A number of approaches have been developed to achieve the controlled administration of biologically active agents via implantation (or insertion) in tissue these approaches are outlined as follows-

1) CONTROLLED DRUG DELIVERY BY DIFFUSION PROCESS
   a) Polymembrane permeation controlled drug delivery system.
      1) Nonporous membranes.
      2) Micro porous membrane.
      3) Semi permeable membranes.

   b) Matrix diffusion controlled drug delivery system.
      1) Lipophilic polymers
      2) Hydrophilic polymers
      3) Porous polymers.

   c) Micro reservoir partition controlled drug delivery system.
      1) Lipophilic membrane with hydrophilic matrix.
      2) Hydrophilic membrane with lipophilic matrix.

2) CONTROLLED DRUG DELIVERY BY ACTIVATION PROCESS
   1) Osmotic pressure activated drug delivery.
   2) Vapour pressure activated drug delivery.
   3) Magnetically activated drug delivery.
   4) Hydration activated drug delivery
   5) Hydrolysis activated drug delivery.

3) CONTROLLED DRUG DELIVERY BY FEEDBACK REGULATED PROCESS
   1) Bioerosion regulated drug delivery.
   2) Bioresponsive drug delivery.[6,9]

POWDERS FOR INJECTION

Powders for injection (PIs) constitute an important category of dosage forms for active molecules. Because of their instability in the aqueous environment, PIs cannot be marketed as ready-to-use injectables [11]. Instead, they are marketed as dry powders to be reconstituted with a suitable vehicle just before administration. The final form after reconstitution may be either a solution or a suspension [12]. Typical molecules in this category include _lactam antibiotics, cephalosporins, and acyclovir. A few ready-to-use infusion products are marketed as frozen solutions in plastic bags for these molecules. However, the low temperature required for their shipment and storage makes these products an unviable option, especially in countries in which a cold chain from manufacturing to
the point of consumption is difficult to establish. The first strategy of lyophilizing (freeze-drying) the primary pack allows the formulation of drugs that are thermolabile or unstable in aqueous solution. However, lyophilisation normally yields an amorphous or partially amorphous product, which leads to solid-state instability [13]. A more-stable crystalline stage can be obtained by crystallisation in aseptic conditions, and it can be maintained by directly filling the sterile dry-powder drug into presterilized vials. The dry-filling process also is much more cost effective because it requires less infrastructure as well as a reduced amount of energy and a shorter amount of time to produce a batch [14].

These reasons have made dry-filled PIs a popular dosage form. A PI formulation may consist of drug only or drug plus excipient. The dry-powder fill approach involves depositing a drug (plus excipient) into individual vials using suitable filling equipment. The entire process does not involve the addition of an excipient or processing step except when two drugs or a drug and an excipient are mixed. Complexities resulting from the presence of an excipient (e.g., interactions with the active molecule and product performance) are absent in PIs containing only the active drug. Formulations containing a drug and excipients also are relatively simple in terms of number and variety of excipients. For this reason, formulation development scientists tend to underestimate the development process of PIs. The molecular level is characterized by the crystal lattice arrangements of the molecules and how they affect properties such as aqueous solubility, dissolution kinetics, hygroscopicity, and chemical stability. A drug can exist in amorphous or crystalline form. Polymorphism is the existence of several crystalline forms of a compound, and it has serious implications on physicochemical properties and product stability [15, 16]. Ashizawa et al. studied various solid forms of an investigational 3 betaine–type cephalosporin, E1040, with respect to chemical stability [17]. Three forms were studied: freeze-dried anhydrous amorphous form, crystalline form, and sodium chloride–additive freeze-dried amorphous form. They found that only the latter two forms were chemically stable during thermal stress.

**ADVANCED PARENTERAL DRUG DELIVERY SYSTEM**

1) **Liposomes**

- Liposomes are formed by the self-assembly of phospholipid molecules in an aqueous environment, the amphiphilic phospholipid molecules form a closed bilayer sphere in an attempt to shield their hydrophobic groups from the aqueous environment while still maintaining contact with the aqueous phase via the hydrophilic head group. The resulting closed sphere may encapsulate aqueous soluble drugs within the central aqueous compartment or lipid soluble drugs within the bilayer membrane. Alternatively, lipid soluble drugs may be complexed with cyclodextrins and subsequently encapsulated within the liposome aqueous compartment. The encapsulation of drugs with liposomes alters drug pharmacokinetics and this may be exploited to achieve targeted therapies. Alteration of the liposome surface is necessary in order to optimize liposomal drug targeting and to achieve prolonged circulation times liposome size between 70–200nm is necessary. Liposomes are the most widely studied modern drug delivery system because of its amazing application for the management of following diseases:

   i) **Liposomal anticancer agent** -

   The use of liposomes as anticancer drug delivery systems was originally hampered by the realization that liposomes are rapidly cleared from the circulation and largely taken up by the liver macrophage. It was observed that doxorubicin loaded stealth liposomes circulate for prolonged periods, accumulate and extravagate within tumours & also improve tumoricidal activity. In one study it has been reported that in patients, liposomal doxorubicin accumulates within Kaposi’s sarcoma lesions and produces a good therapeutic response. Liposomal doxorubicin is now licensed as Caelyx, for the treatment of Kaposi’s sarcoma. This formulation is currently in clinical trials for ovarian cancer and could be approved shortly for use in ovarian cancer patients who have failed to respond to paclitaxel and cisplatin.

   ii) **Liposomes as vaccine adjuvants** -

   Liposomal vaccines can be made by associating microbes, soluble antigens, cytokines or deoxyribonucleic acid (DNA) with liposomes, the latter stimulating an immune response on expression of the antigenic protein. Liposomes encapsulating antigens, which are subsequently, encapsulated within alginate lysine microcapsules to control the antigen release and to improve the antibody response. Liposomal vaccines may also be stored dried at refrigeration temperatures for up to 12 months and still retain their adjuvanticity.

   iii) **Liposomal anti-infective agents** -

   Liposomal amphotericin B (Ambisome), used for the treatment of systemic fungal infection. This is the first licensed liposomal preparation. It was observed in one study that liposomal amphotericin B, by passively targeting the liver and spleen, reduces the renal and general toxicity of the drug at normal doses.

2) **Niosomes:**

- Niosomes are unilamellar or multilamellar vesicles, where in an aqueous solution is enclosed in highly ordered bilayer made up of nonionic surfactants with or without cholesterol (chol) and dicetyl phosphate and exhibit a behavior similar to liposomes in-vivo. They can be used in the treatment of cancer and also used as vaccine adjuvant. Some of its applications are:

   i) **Anticancer niosomes** -

   Anticancer niosomes, if suitably designed will be expected to accumulate within tumours. For example niosomal encapsulation of methotrexate and doxorubicin increases drug delivery to the tumour and tumoricidal activity. It was reported that
doxorubicin Niosomes having size 200nm with a polyoxyethylene (molecular weight 1,000) surface are rapidly taken up by the liver and accumulate to a lesser extent in tumour, this technology may prove advantageous for the treatment of hepatic neoplasms. It was also observed that the activity of other anticancer drugs, such as vincristine, bleomycin, plumbagin and a plant derived anticancer agent are improved on niosomal encapsulation.

ii) Niosomes at targeted site-
Uptake by the liver and spleen make niosomes ideal for targeting diseases manifesting in these organs. One such condition is leishmaniasis and a number of other studies has shown that niosomal formulations of sodium stibogluconate improve parasite suppression in the liver spleen and bone marrow. Niosomes may also be used as depot systems for short acting peptide drugs on intramuscular administration.

iii) Niosomes as vaccine adjuvants—
It was studied that niosomal antigens are potent stimulators of the cellular and humoral immune response. The formulation of antigens as a niosome in water-in-oil emulsion further increases the activity of antigens and hence enhanced the immunological response.

3) Nanoparticles and Microparticles:
Nanoparticles and microparticles are usually prepared by the controlled precipitation of polymers solubilised in one of the phases of an emulsion. Precipitation of the polymer out of the solvent takes place on solvent evaporation, leaving particles of the polymer suspended in the residual solvent. For particulate dispersions, the required particle size of nanoparticles lies between the range of 30-500nm while for microparticles in excess of 0.5micron. Their applications in management of diseases are:

i) Tumor targeting nanoparticles and microparticles
The accumulation of non-stealth doxorubicin nanoparticles within the Kupffer cells of the liver may be used to target hepatic neoplasms indirectly, this is achieved by providing a depot of drug for killing nearby neoplastic tissue. Microparticles may also be injected directly into tumours. It was observed that the direct injection of microparticles into solid tumours increases the tumoricidal activity of the drugs 5- fluorouracil and doxorubicin.

ii) Vaccine adjuvants-
Nanoparticles have also been used as vaccine adjuvants. It was reported that antigens, which adsorbed onto the surface or entrapped in the matrix of polymethylmethacrylate nanoparticles induces an enhanced immunological response. For example polymethylmethacrylate nanoparticles containing the influenza antigen may protect people against disease to a greater extent than the antigen alone.

iii) Other applications-
Restenosis, defined as the re-obstruction of an artery following procedures such as angioplasty or artherectomy may be treated by the local application of dexamethasone-loaded polyactic acid co-glycolic acid nanoparticles. Cyclosporin A, an immunosuppressant drug used to prevent graft rejection after transplantation by the inhibition of T-lymphocytes, may be targeted to regional lymph nodes by the intramuscular administration of cyclosporin A polyactic acid nanoparticles. In short it can be said that, by virtue of their small size solid nanoparticles provide opportunities for targeted parenteral therapies and may also be used as immunoadjuvants.

4) Prodrugs -
A prodrug is a pharmacological substance, which is administered in an inactive form. Once administered, it is metabolized in the body in vivo into the active compound. The use of prodrugs in cancer chemotherapy as a means of targeting relatively toxic compounds to specific areas of pathology is enjoying renewed activity. Two of the technologies being evaluated at present are antibody directed enzyme prodrug therapy (ADEPT) and the use of polymeric prodrugs.

i) ADEPT
an antibody-enzyme conjugate is administered intravenously, localizes in tumour tissue and subsequently activates an administered prodrug predominantly within such tumours. Prodrug activating enzyme is carboxypeptidase G2.

ii) Polymeric prodrugs -
This involves the use of an active substance and possibly a targeting moiety, both linked viaam spacers to a water-soluble polymeric backbone. From this basic blueprint a number of polymer drug conjugates used for cancer chemotherapy and have been synthesized with cleavable drug polymer linkers. These include soluble polymeric prodrugs of daunorubicin, doxorubicin, cisplatin and 5-fluorouracil. Passive tumour targeting with polymer drug conjugates improves the tumoricidal activity of anticancer agents. Distribution to potential sites of toxicity, such as the distribution of doxorubicin to heart tissue, is also decreased with polymer drug conjugates. In short, polymer drug conjugates have progressed from an elegant scientific concept to the clinic and may result in a new form of therapeutics for routine use.[18,19,20,21]
RECENT INNOVATIONS IN STERILE DRUG DELIVERY DEVICES

Needle free Injection Devices

Crossject has developed a range if needle-free injection devices for sub-cutaneous, intramuscular or intradermal routes. The device reconciles all ‘needle phobics’ with injections. It eliminates the risk of needle-stick injury and needle contamination, and thanks to its ease of use, it improves patient quality of life.

Inter-Vial Plus - A reconstitution device:

Dujoect's INTER-VIAL PLUS™ system is a technologically advanced, simple to operate, closed system designed to safely, precisely and intuitively dissolve or suspend and deliver a solid dose drug such as a protein or peptide compound. An important variation in the design of Dujoect's INTER-VIAL PLUS™ system has been to reverse the traditional position of the wet and dry chambers of our Inter-Vial system. Since the drug admixture is not transferred between the chambers, transfer losses are nil. The drug reconstitution is performed in its original container (a syringe) and delivered to the patient from this same container. The wet chamber consists of a prefilled vial which can contain Sterile Water for Injection conforming strictly to USP, EP or JP. Other than the added benefits with the reversed chambers, the INTER-VIAL PLUS™ and the.

Insulin Pen Injectors - typical dosing range: 0.01–0.6ml (1–60 I.U)

Insulin pens are reusable or disposable multi-dose injectors for frequent injections designed for dedicated 3ml cartridges and pen needles. All Ypsomed’s insulin pens include easy dose-setting and clear last-dose indication for when the cartridge is nearly empty. For reusable devices simple cartridge exchange is essential. Above all the dose display must be large and easy to read, while the device itself needs to suit the target patient group. With most current devices the injection process (needle insertion and injection) is performed manually. Spring aided injection can provide benefits to patients.

Pen Injectors for Other Indications Typical dosing range: 0.05–0.5ml

Ypsomed has a range of pen devices to cover frequent injection therapies such as hGH, FSH, GLP-1 and PTH. Some of these therapies require a fixed dose whereby the device must clearly communicate that the dose has been set and injected. Other therapies benefit from dose-memory functions which simplify handling so that the patient only needs to set the required dose once for each new cartridge. All pen platforms are designed to accommodate a single-chamber (liquid-stable) or a dualchamber cartridge.

Monodose Pens for Dual-Chamber Cartridges

Many new Injectable therapeutics are available only as lyophilized formulations where a dualchamber cartridge is required and the device is disposed of after a single injection. The use of dual-chamber cartridges puts special demands on the pen system in terms of intuitive reconstitution, priming and dose-setting steps. It is very important for the patient that these steps are easy to learn and always performed in the correct order.

Disposable Auto-Injectors Typical dosing range: up to 1ml

Disposable auto-injectors are typically single-dose delivery devices used for the infrequent injection of larger doses of drugs of different viscosities. The standard device is designed for 1ml long pre-filled syringes. The complete injection process (needle insertion, injection and subsequent needle shielding) is performed automatically. Ease of use, full needle safety and clear injection feedback are standard features of Ypsomed's auto-injectors.

Pens With Replaceable Cartridges:

Insulin cartridges for pens come in 3.0 ml and 1.5 ml sizes, with 3.0 being the predominant size.

Prefilled Pens:

Pens that come with a prefilled insulin cartridge are thrown away when the insulin is used up. Prefilled pens using pre-mixed insulin are usually marketed for use by people with type 2 diabetes.

A Pen with a memory:

"HumaPen MEMOIR is the first and only insulin pen with a memory. HumaPen MEMOIR records the date, time, and amount of your last 16 doses (including priming doses). You can see exactly when and how much insulin you last took. With HumaPen MEMOIR, you simply "dial" your dose by turning the dose knob in one-unit increments (up to 60 units) after initial set-up. If you dial too many units, you can correct the dose without wasting any insulin. HumaPen MEMOIR is a reusable pen for use only with Humalog (insulin lispro injection [rDNA origin]) 3 mL insulin cartridges.[22]

FUTURE SCOPE

Many pharmaceutical manufacturers coming forward to formulate parenteral dosage form due to its beneficial characteristics over other conventional dosage forms. The dry-filling process also is much more cost effective because it requires less infrastructure as well as a reduced amount of energy and a shorter amount of time to produce a batch. These reasons have made dry-filled PIAs a popular dosage form. In future prefilled syringes of these powder for injection may be formulated. In the future, the pharmaceutical and biotech industries will ask for prefillable drug delivery systems for valuable potent drugs.

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