INTRODUCTION

In a Controlled Release Drug Delivery System the release of the active material may be constant or cyclic over a long period, or it may be triggered by the environment. In any case the purpose behind controlling the drug delivery is to achieve more effective therapies while eliminating the potential for both under and overdosing.

CRDDS are also known as delayed release, sustained action, prolonged action, sustained release, prolonged release, time release, slow release, extended release forms.

An ideal CRDDS should be inert, biocompatible, mechanically strong, comfortable for patient, capable of achieving high drug loading, safe from accidental release simple to administer and remove, easy to fabricate and sterilize.

Advantages

Maintenance of drug level within the desired range, fewer problem with patient compliance, the need of fewer administrations, use of less total drug, minimal drug accumulation with long term dosage, improved treatment efficiency, more rapid control of patient condition, less fluctuation in drug level, increased safety margin of high potency drug due to better control of plasma level.

Disadvantages can not be ignored

Decreased systemic availability in comparison to immediate release conventional dosage forms, possible toxicity or non-biocompatibility of the material used, undesirable byproducts of degradation, surgery required to implant or remove the system. The chance of patient discomfort from drug delivery device, high cost of these formulations, polymer Drug interactions, possibility of dose dumping thus increased toxicity risk, poor in-vitro-in-vivo correlation.

Need of Controlled Release Drug Delivery System

Where traditional formulations fail they can be used: situation requiring: the Slow release of water soluble drugs, fast release of low solubility drugs, drug delivery to specific sites, drug delivery
using nano particulate system, delivery of two or more agents with the same formulation.

**Factors influencing the design of CRDDS**

Physiochemical properties of drug such as solubility, stability, partition coefficient, charge and protein binding. Rate of administration plays important role, its role should be considered. Acute/chronic therapy is an important factor controlling design of CRDDS like development of one year contraceptive implant represents a different case than does an antibiotic treatment for acute microbial attack. Target site: untoward side effects can be minimized by delivering the maximum fraction of applied dose reaching the target site. Condition of patient, whether in ambulatory bedridden, obese or gaunt, old or young etc, can effect the design of control drug delivery.

**Polymers used in control release medications**

Materials must be chemically inert and free from leachable impurities appropriate physical structure, minimal undesired aging, readily processable, they include: Poly(2-hydroxy ethyl methacrylate), poly(N-vinyl pyrrolidone), poly (methyl metha crylate), Poly (vinyl alcohol), Poly acrylamide, poly (ethylene-co-vinyl acetate, poly (ethylene glycol), poly (methacrylic acid).

Additional polymers for medical application, they are designed to degrade within the body, among them, polylactides (PLA), Poly glycolides, (PGA), Poly (lactide-co-glycolides) PLGA, polyanhydrides, poly-orthoesters.

**Factors affecting Biodegradation of Polymers**

Chemical structure, chemical composition, distribution of repeat units in monomers, presence of ionic group, presence of unexpected units or chain defects, configuration structure, molecular weight, Molecular Weight distribution, morphology (amorphous/semicrystalline, microstructures, residual stresses), presence of low molecular weight compounds, processing conditions, Annealing, sterilization process, storage, history, shape, site of implantation physichochemical factors (ion exchange, ionic strength, pH) Physical factors (shape and size changes, variation of diffusion coefficients, mechanical stress), mechanism of hydrolysis (enzyme versus water).

**Control Release Mechanism**

There are three primary mechanism by which active agents can be released from a delivery system: diffusion, swelling and degradation followed by diffusion. **Diffusion:** It can occur on a macroscopic scale through pores in the polymer matrix or on a molecular level, by passing between polymer chains. As the release continues, its rate normally decreases with this type of system, since active agent has a progressively longer distance to travel and therefore requires a longer diffusion time to release.

**Stimulus Hydrogel Mechanism**

It involves hydrogel change in pH-swelling- release of drug or ionic strength Ionic hydrogel change in ionic strength- change in concentration of ions inside gel- change in swelling-release of drug or electrically it can be hydrogel applied electric field-membrane charging electrophoresis of charged drug-change in swelling-release of drug.

**Bio Degradable Systems**

Most of Biodegradable polymers are designed to degrade as a result of hydrolysis of the polymer chains into biologically acceptable and progressively smaller, compounds. For example polylactides, polyglycolides and their co-polymers the polymer will eventually break down to lactic acid and glycolic acid enter the kreb's cycle and further breaker down into carbon-di-oxide and water and excreted through normal process.

**Types of Controlled-Drug Delivery**

Sustained release form can be grouped according pharmaceutical mechanism. (a) Osmotic system include the Oros system (Alza) which is an oral osmotic pump composed of a core tablet and a semipermeable coating that has a small hole (0.4mm in diameter) for drug exit. Hole is produced by laser beam. (b) Coated beads or granules produce a blood level profile similar to that obtained with multiple dosing (c) Microcapsules are formed by micro encapsulation by which solid, liquid or gases are encased in microscopic
capsules. Two techniques have been employed for micro encapsulation (i) coacervation (ii) Film forming (shellac, wax, gelatin, starch) (d) Matrix tablets use insoluble plastics (e.g. polyethylene, polyvinyl acetate, polymethacrylate) or hydrophillic polymers (methyl cellulose, HPMC) or fatty compounds (various waxes, glyceryl stearate). The most common method of preparation is mixing of the drug with the matrix material followed by compression of the material into tablets (e) Ion exchange resins can be complexed with drugs by passage of a cationic drug solution through a column that contains the resins. The drug is complexed to the resin by replacement of hydrogen atmos. Example include lanamin capsules. (f) Complex formation is used for certain drug substances that combine chemically with other agents. Example: Hydroxypropyl- B cyclodextrin form a chemical complex that can be only slowly soluble form body fluids depending upon the pH of the environment.

**Future Directions in controlled drug delivery**

The most exciting opportunities in Controlled Drug Delivery lie in the arena of responsive delivery systems, with which it will be possible to deliver the drugs through implantable devices in response to a measured blood level or to deliver the drug precisely to the targeted site. Much of the development of novel materials in Controlled Drug Delivery such system include:

- Block or graft co-polymer, complexation network responding via hydrogen or ionic bonding,
- Dendimers or star polymers as nanoparticles for immobilization of enzymes, drugs, peptides or other biological agents.

New blend of hydrocolloids and carbohydrate based polymers. These new biomaterial-tailor-made copolymers with desirable functional group are being created by researchers who envision their use not only for innovative Controlled Drug Delivery System but also as potential linings for artificial organs, as substrates for cell growth or chemical reactors, as agent in the drug targeting and immunology testing as biomedical adhesive and bioseparation membranes and substances able to mimic biological systems.

**REFERENCES**
