INTRODUCTION:

Evolution of an existing drug molecule from a conventional form to a novel delivery system can significantly improve its performance in terms of patient compliance, safety and efficacy. Drug delivery companies are engaged in the development of multiple platform technologies for controlled release, taste-masking, oral fast dispersing dosage forms, technology for insoluble drugs, and delivery of drugs through intranasal, pulmonary, transdermal, implant, vaginal, colon, and transmucosal routes to get competitive advantage, extend patent life and increase market share of their products. The market for innovative drug delivery systems involving industrially feasible, cost effective and advanced technology is gaining importance.

Implantable dosage forms are useful for patients having difficulty in taking drugs orally, and allow the avoidance of frequent dosage by sustained supply. A simple administration such as the injection of a drug solution sometimes causes toxic side effects due to a temporary but excessive drug concentration. Further, in the case of time-dependent drugs, as it is therapeutically essential to maintain the drug concentration above the effective lower limit for a long time, excessive drug concentration is not needed. Implants are one of the dosage forms used to achieve effective concentrations for a long time for such time-dependent types of drugs. The base materials for implants are required to be biocompatible. Biodegradable and non-biodegradable polymers are often utilized as a base material. Non-biodegradable polymers have to be taken out surgically after completion of the drug release, resulting in pain and a burden on patients. On the other hand, as biodegradable polymers disappear spontaneously from the body during or after drug release, their implants are superior in lowering the burden on patients.

IMPLANTABLE DRUG DELIVERY SYSTEM (IDDS):

Implants are defined as sterile solid drug products made by compression or melting and mainly consist of drug and rate controlling excipient.

USP XXIII has defined implants as “pellets of small sterile solid masses consisting of a highly purified drug (with or without excipient) made by compression molding” they are intended for implantation in the body (usually subcutaneously) for the purpose of providing continuous release of the drug over long period of time.
ADVANTAGES OF IDDS:

1) Improved control of drug levels at site of action.
2) Drugs are delivered as near as possible to their target site of action and undesirable effects on other organs are
3) IDDS’s help in protection of drug that are rapidly metabolized or have short \textit{in vivo} half-life.
4) Improved patient compliance is particularly beneficial for patients who abuse drugs and have compliance problem during treatment.
5) Immediate removal of implant is possible, in contrast to parenteral, in case of certain allergies or side effects.
6) Maintenance of constant plasma drug concentration for a desired period of time.
7) Reduction in cost of therapy.

DISADVANTAGES OF IDDS:

1) Toxicity or lack of biocompatibility of materials used for implants.
2) Formation of harmful byproducts from implants.
3) Minor surgery is required for implantation, and also to remove it from administered site if the implant is not biodegradable.
4) Pain and discomfort may be caused by implantation.
5) Expensive due to cost of polymers, pump or manufacturing procedure.
6) Leak or bursting leading to imprecise drug release.

THERAPEUTIC AGENTS SUITABLE FOR IMPLANTABLE DRUG DELIVERY:

The therapeutic agents that are suitable for biodegradable drug delivery systems are those that

(a) Need to be administered for long period of time
(b) Are highly potent and have a low dose
(c) Have a short biological half life
(d) Have compliance issues
Historically, the subcutaneous implantation of drug pellets is known to be the first biomedical approach aiming to achieve the prolonged and continuous administration of drugs. This first generation of IDDS was produced by compressing drug crystals, with or without small fraction of pharmaceutical excipients, into small cylindrical solid pellets that could be readily implanted into subcutaneous tissue by means of pellet injector or by making a small skin incision.

Over the years a number of approaches have been developed to achieve the controlled administration of biologically active agents via implantation or insertion in tissues. Many different types of polymeric systems are available for controlling the release of drugs in various types of drug delivery system. Drug release from most Implantable devices is controlled by any one of the following approaches as discussed below.

Drug release from Implantable drug delivery

- Diffusion
- Chemically
- Externally
- Self

Controlled Systems
- Membrane permeation
- Biodegradable systems
- Magnetically activated Ionic strength
- Ultrasonically
- Thermally activated

Controlled Systems
- Solvent
- Regulated

Regulated Systems
OSTEOMYELITIS: 6, 7

Osteomyelitis is such an historic infection which is still remains challenging and difficult to treat, despite of advances in antibiotics and new operative techniques. Osteomyelitis, either acute or chronic, is an inflammatory bone disease caused by pyrogenic bacteria. Osteomyelitis is defined as progressive infection of bone or bone marrow and surrounding tissues. The root words osteon (bone) and myelo(marrow) are combined with itis(inflammation) to define the clinical state in which bone is infected with microorganisms. It is mainly characterized by inflammation and swelling of bone tissues.8

It is also called as multibacterial bone infection because it is caused by variety of microorganisms. Staphylococcus aureus(80-85%) is the major organisms associated with osteomyelitis. Infection is more common in the long bones and vertebras of the body, but it can also affect other bones in the body.9,10

The incidence of the disease is high in both developed and developing countries. Chronic osteomyelitis is observed in about 2 in 10,000 adults.11 Children’s and infants are more prone to disease than adults; about 2 in 5,000 children’s and 1 in 1,000 infants are affected by acute osteomyelitis. People who have diabetes, who have had a traumatic injury recently, or uses intravenous drugs are at greatest risk for chronic infection. In spite of advances in antibiotic therapy, bone infections continue to cause significant morbidity from residual damage and chronic recurring infections.

CAUSES OF OSTEOMYELITIS: 5, 12-15

Osteomyelitis occurs due to following reasons:

1. Osteomyelitis may occur as a result of a bacterial bloodstream infection, sometimes called bacteremia, or sepsis, that spreads to the bone. This type is most common in infants and children and usually affects their long bones such as the femur (thighbone) or humerus (upper arm bone). When osteomyelitis affects adults, it often involves the vertebral bones along the spinal column.
2. Osteomyelitis may occur as a result of a nearby infection due to a traumatic injury, open fractures, frequent medication injections, a surgical procedure, or use of prosthetic devices.

3. Osteomyelitis may also occur as a result of bacterial intruders which travel from other parts of the body, such as the ear, throat, intestinal or urinary tract infection, through the bloodstream and to a bone, where they can start an infection.

4. Osteomyelitis may also occur as a result of extension of a contiguous spread of infection. e.g. from an overlying ulcer of the skin, burns, sinus disease.