The Biodegradable Pills : An innovative approach

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Abstract: *There are various advantages of biodegradable pills controlled drug delivery methods over other techniques which help to make it successful delivery system. It is a novel method of incorporating drug in microencapsulation having tremendous scope and various applications. The various drug therapies and types of drugs demand different formulations, fabrications conditions and release kinetics. There is no single polymer can satisfy all the requirements. Therefore, there have been various advances in area of biodegradable copolymers over the last 30-40 years. This article reviews current research on biodegradable polymers, focusing their potential as drug carries. The major classes of polymers are briefly discussed with regard to synthesis, properties and biodegradability, and known degradation pattern. A vast majority of perishable polymers studied belongs to the polyester family, which includes polyglycolides and polylactides. Other degradable polymers such as polyorthoesters, polyanhydrides and polyphosphazenes are also discussed in the biodegradable drug delivery system.*

Key Words: *Gastrointestinal, Oral drug delivery, microneedles, Biodegradable pills, Fabrication techniques of biodegradable pills , Mechanism of Pills Degradation.*

1. INTRODUCTION:

Biodegradable polymers are firstly developed in requirement for biodegradable suture materials and have been proven to be useful and successful for long-term drug delivery applications. These polymers are highly desirable in these situations because they degrade in the body to biologically inert and compatible molecules. By incorporating drugs in biodegradable polymers, dosage forms that release the drug over a prolong length of time can be prepared in variety of shapes and sizes.[1] No surgical procedures are required once completion of indefinite quantity regime since the remaining chemical compound can degrade and find cleared by the body. Polymers are macromolecules having the massive chains contain a numerous useful teams, can be mixed with lower and higher molecular weight materials. Polymers become more and more necessary within the field of drug delivery. Advances in the chemical compound science have light-emitting diode to the many novel drug delivery systems. A proper thought of surface and bulk properties will aid within the planning of polymers for numerous drug delivery applications. These new technology shows drug modification by chemical which suggests that, career based drug delivery system and drug entrapment in polymer matrices or within the pumps that are placed in desired body compartments. And the human health is improved by these technical developments in drug delivery approaches. Use of the compound material in novel drug delivery approaches has attracted the various scientist which will use this technique later on for research purpose.[2] .

1.1 Need for using biodegradable pills:

It was identified that the surgical removal of the drug depleted delivery system was difficult, leaving Non-biodegradable foreign materials in the body for the indefinite time period caused toxicity problem. While diffusion of controlled release is an excellent means of achieving system. Several approaches have been shown in an attempt to enable oral administration of biologics, including co-administration with the enzyme inhibitors,[3] chemical modification of the drug, polymer micro- and nanocarriers, liposome carriers, as well as targeted nanoparticles. There is no need for a second surgery for removal of the Polymers. Avoid the stress shielding. Provide tremendous potential because of the basis for controlled drug delivery.[4]

1.2 Advantages:

- Avoid first pass hepatic metabolism in comparison to other oral drug delivery systems.
- It also avoids gastrointestinal absorption and enzymatic or pH related deactivation, avoids gastrointestinal irritation and reduces fluctuations in plasma drug profile.[4]

- It enhances bioavailability as well as the high concentrations of drugs delivered via this route which can be localized at the site of action, thereby reducing the systemic drug levels and also reducing the systemic side effects associated with the drug.
- It is an attractive method to transport drug or biological compounds due its advantage in reducing the pain and inconvenient intravenous injections.
- It has convenient route and can deliver therapeutic volumes/ doses of drug quickly with minimal discomfort.
- It is simple, inexpensive and self administrable.
- It can create sustained or bolus delivery profiles.
- It has rapidly responsive pharmacokinetics and pharmacodynamics.
- It provides drug at a constant controlled rate over a prescribed period of time.
- The polymer carrier would degrade into nontoxic, absorbable subunits which would be subsequently metabolized.
- The system would be biocompatible would not exhibit dose dumping at any time and polymer would retain its characteristics until after depletion of the drug.
- Degradable system eliminates the necessity for surgical removal of implanted device following depletion of a drug.
- They are break down into biologically acceptable molecules that are metabolized and removed from the body via the normal metabolic pathways.
- Ability to change surface chemically and physically.
- Ability to immobilize cells or biomolecules within them or on the surface (Drug Eluting Stent).
- It provides a drug at a constant rate of controlled release owes a prescribed period of time.
- The polymer carrier would degrade into nontoxic and absorbable subunits which would be subsequently metabolized.
- The system would be biocompatible would not exhibit dose dumping at any time period and polymer would retain its characteristics until after depletion of the drug.
- Biodegradable system eliminates the necessity for surgical removal of implanted device following depletion of a drug.
- They are broken down into biologically acceptable molecules that are metabolized and removed from the body through normal metabolic pathways.[5]

1.3 **Disadvantages:**

- Systems containing tiny sized molecules will solely simply penetrate the skin.
- It possesses native irritation, erythma, itching, and native hydrops is also produces by the drug or alternative excipients at the positioning of application within the patch formulation.
- Restricted porousness across the skin could limit the delivery of variety of medication.
- Typically the degradable polymers exhibit substantial dose marketing at some purpose.
- A “burst effect” or high initial drug unharness shortly when administration is typical of most system.
- Biodegradable systems which are administered by injection of a particulate form are non- retrievable.
- Presence of substances that may be issued in the body monomers (toxic), catalysts, after degradation.
- Ease of water and biomolecules absorption from surrounding.
- Low mechanical properties.
- In some cases, difficult to sterilization.
- Sometimes the biodegradable polymers exhibit substantial dose dumping at some point.[8]

2. BIODEGRADABLE PILLS :

It has been recognized that some important new therapeutic drug entities will be difficult to successfully administer via the oral route because of molecular size or chemical/physical instabilities that occur within the gastrointestinal tract. Specifically, the peptides drugs are a prime example of these new and rather important entities. In recent years, significant research attention has been turned to the development of pharmaceutical techniques that could facilitate successful oral absorption of peptide drugs. In general, most of these techniques either utilize mechanical protection to shield the peptide molecule from the hostile gastrointestinal environment, or combine protection with a variety of techniques to increase the absorption potential of these difficult-absorb drug molecules. Unfortunately, the published reports regarding these techniques indicate that difficulty in achieving significant levels of absorbed drug after oral administration still remains. A careful analysis of the problems inherent in the oral delivery of peptide will yield a number of rather troublesome facts:

1. Peptides do not diffuse well across biological membranes .
2. Peptides are easily destroyed by hostile gastrointestinal juice and enzymes.
3. Peptides , as a class, exhibit poor water solubility , or tend to "associate" in solution, limiting the extent of an absorption pool that would be necessary for sufficient membrane transport.[3]

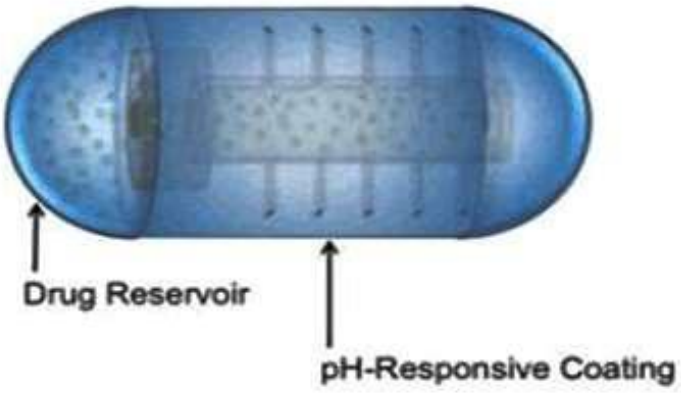

Fig 1: Biodegradable pill

2.1 Mechanism of working and design of Biodegradable pills:

Scientists have tried coming up with microparticles and nanoparticles which will deliver biologics, however such particles area unit high-priced to provide and need a replacement version to be built for every drug. Schoellhammer, Traverso, and their colleagues taken off to style a capsule that may function a platform for the delivery of a good vary of medicine, forestall degradation of the drugs, and inject the payload directly into the liner of the digestive tract. The polyacrylic prototype capsules, 2 centimeters longer and 1 centimeter in a diameter wise, which is includes a reservoir for the drug and is coated with the hollow, stainless steel needles which is about 5 millimeters long. Previous studies of accidental intake of the sharp objects in human patients who have urged that it can be safe to swallow a capsule coated with short needles. Because there are not a pain receptors within the digestive tract, patients wouldn't feel any pain from the drug injection. To test whether or not this sort of capsule might enable safeer and effective drug delivery, the researchers tested it in pigs, with hypoglycemic agent because the drug payload. It took quite per week for the capsules to maneuver through the complete GI tract, and also the researchers found no traces of tissue injury, supporting the potential safety of this novel approach. They conjointly found that the microneedles with success injected hypoglycemic agent into the liner of the abdomen, small intestine, and colon, causing the animals' blood glucose levels to drop. This reduction in blood sugar was quicker and bigger than the drop seen once identical quantity of hypoglycemic agent was given by injection. "The dynamics area unit far better, and much faster-onset, than those seen with traditional under-the-skin administration," Traverso says. "For molecules that area unit notably tough to soak up, this would be a way of actually administering them at much higher efficiency." "This is a very interesting approach," says Samir Mitragotri, a academic of chemical engineering at the University of Golden State at town UN agency wasn't concerned within the analysis. "Oral delivery of medication could be a major challenge, especially for protein drugs. There is tremendous motivation on various fronts for finding other ways to deliver drugs without using the standard needle and syringe." Safety Evaluation of a Microneedle Prototype in the GI Tract The safety and talent for natural passage of a microneedle containing device via the digestive tract was investigated. Safety and passage time was calculable exploitation the customised device. The dimensions of this prototype were modeled around those of US FDA-approved ingestible devices, such as the video capsule endoscope. The microneedles were placed radially around the device to ensure greatest apposition of the needles with the GI mucous membrane. A metal core was added to aid in the visualization of the pill on radiographs. The device was endoscopically deployed within the abdomen of 3 animals. Animals were monitored daily and radiographs were taken to track the pill movement and to monitor for any evidence of intestinal obstruction or perforation. Throughout the transit time of the epitome, all animals remained free of clinical signs of obstruction. Furthermore, radiographs remained free of evidence of intestinal obstruction or perforation. Loss of a detectable radiopaque device on the radiographs was used to determine the approximate transit time of the prototypes. The passage time of the device in 3 completely different animals was 7, 19, and 56 days. Upon loss of the radiopaque device, animals were euthanized, and the entire GI tract was examined and found to be macroscopically normal. Further, the three sites of constriction in the GI tract distal to the site of prototype deployment (pylorus, ileocecal valve, andanal canal) were examined and appeared normal. Additionally, these three points were also fixed in formalin for histological examination. Histological examination was notable for normal appearing tissue at all three sites of constriction in the GI tract in the three animals.[6]

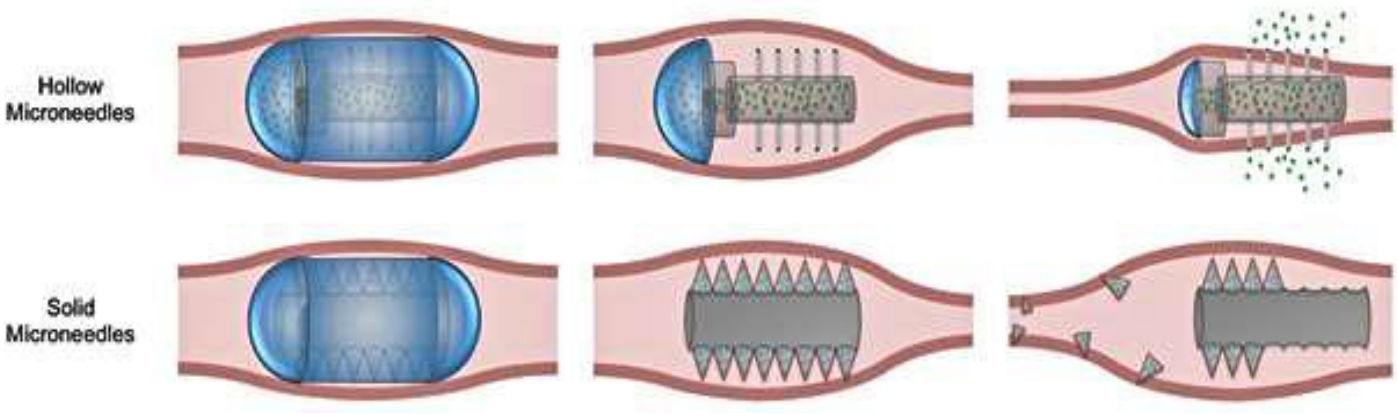

Fig 2: Mechanism of working of biodegradable pill

2.2 Mechanism of Degradation:

The term degradation designates the process of polymer chain cleavage which leads to a loss in molecular weight. Biodegradation of the aliphatic polysters occurs by bulk erosion .The lactide/glycolide polymer chains are cleaved by hydrolysis to the monomeric acids and are eliminated from the body through the Krebs cycle, primarily as carbon dioxide and in urine. Because the rate of hydrolysis of the polymer chain is dependent only on significant changes in temperature and pH or presence of catalyst, very little difference is observed in rate of degradation at different body sites. This is obviously an advantage in regard to drug delivery formulations.[4] Degradation induces the subsequent erosion of the material which is defined as mass loss of material. The former involves degradation all over the cross section because of water penetration followed by slow scissions of long polymer chains, while the latter is a surface phenomenon. The rate of surface erosion depends on the area exposed to the hydrolytic environment and the rate of bulk erosion depends on the crystalline nature and porosity of the polymer matrix. The drug release pattern from the polymer matrix of microspheres and implants follow the following three step process, that is an initial burst release due to dissolution of surface drug, followed by slow release due to degradation-dependent network relaxation that creates sufficient free volume for drug dissolution, and finally accelerated drug release. The accelerated drug release is triggered by the acidic microenvironment within particle generated by the autocatalytic degradation of the polymers into lactic and glycolic acids. Overall, the release profile is dependent on the nature of the drug, polymer degradation rate, water permeability and drug-polymer matrix interaction. Once degraded, the solubilized momomers/oligomers such as lactic acid and glycolic acid are excreted by the kidney and finally metabolized into carbon dioxide and water through the tricarboxylic acid (Kreb's) cycle . Various advanced analytical techniques are generally useful to understand and illustrate the polymer degradation mechanisms. A simple but relatively effective technique to characterize the degradation of a polymeric matrix is by recording the loss of mass during the degradation process. In most cases the main parameter used for monitoring degradation are changes in molecular weight, crystallinity, pH and thermal changes inside the core.[4]

2.3 Biodegradable polymer:

A perishable compound could be a compound within which the degradation results from the action of present microorganisms like bacterium, algae or fungi. Polymers were initial developed within the search of perishable structures and their applications were found to be helpful and flourishing for future drug delivery. Biodegradable polymers square measure extremely fascinating within their conditions as they degrade in the body to biologically inert and compatible molecules. By incorporating drug into the perishable polymers, the dosage forms releases the drug for a long period of time and can be prepared in variety of shapes and sizes. There is no want of any surgical procedures when the completion of the dosing program, as the remaining polymer form will be degraded and cleared by the body. Many different chemistries for perishable polymers are projected. One of the foremost common and flourishing polymers square measure the polyesters that were initial investigated as perishable sutures. These polymers embody poly (glycolide), poly (D, L-Lactide), and their connected copolymers poly (D, L-lactide – co-glycolide). Preparation of assorted dose forms were administered by several strategies, by simply incorporating the drug directly into the polymer matrix peptides, proteins and genetic and cell based drugs plays a bigger role on the performance because the effective delivery of recent drug therapies of the compound platform. A wide form of delivery systems are developed for the aim of prolonging the discharge and eventually bioavailability of medication to the body. Examples embody the

pad, oral dosage forms such as osmotic pumps and swellable hydrophilic polymer matrices and various types of polymer–based parenterals.[1]

Classification of biodegradable polymers

Biodegradable Polymers square measure macromolecules having terribly giant chains contain a range of useful teams, can be blended with low and high molecular weight materials. Polymers have become more and more necessary within the field of drug delivery. Advances in compound science have semiconductor diode to the event of many novel drug delivery systems.[4]

Polymers are classified into the following types as mentioned below

(a) Polyester: Poly lactic acid, Poly glycolic acid, Poly hydroxyl butyrate, Polyester, Polycaprolactone, Poly lactide-co-glycolide (PLGA), Poly diaxonone.
(b) Polyanhydride: Poly adepic acid, Poly sebacic acid
(c) Polyamides: Poly amino acid, Poly imino carbonate
(d) Phosphorous based polymer: Polyphosphates, Poly phosphonates, Poly Phosphazenes
(e) Others: Poly cyanoacrylates, Poly urethanes, Poly ortho ester, Polyacetals etc.[6]

Properties of biodegradable polymers

A crucial property of biodegradable polymers, biocompatibility is the ability of material contained in specific application to elicit adequate natural physiological reaction of the organism that has to be maintained uninterruptedly for the whole period of therapy. In contrary, chemical, physical and mechanical properties of biodegradable material can change in time and the biocompatibility of degradation products can be different from the biocompatibility of original polymer matrix.[9]

Biodegradable Polymers as Drug Carriers :

A polymer is a large molecule composed of many smaller units called monomers that are bonded together. In addition to eliminating the necessity of removal, the five key advantages that polymeric drug delivery products can offer are; localized delivery of drug, sustained delivery of drug, stabilization of the drug, release rate which is less dependent of the drug properties and steadier release rate with time. In diffusion controlled systems the release rate typically declines with time. On the other hand, a biodegradable system may yield a constant release even with a simple monolithic device if matrix degradation can compensate for this decline, perhaps with an increase of drug permeability.[10]

Biodegradable polymer has to meet following elementary requirements:

- Polymer has to be manufactured from compound that is soluble in water.
- Polymer has to be non-toxic and free of endotoxins so as to minimize undesired reaction of the organism to foreign body or molecule.
- The time necessary for material breakdown should be similar to the expected tissue recovery time or required therapeutic time.
- Degradation products have to be non-toxic and their elimination from the organism has to be easy.
- Mechanical properties have to be suitable for desired role and the product has to be easy to manufacture.
  Other properties of polymer materials that can have impact on their biocompatibility include chemical structure, molecular weight, crystallinity, solubility, hydrophilicity/hydrophobicity, slipperiness, surface chemistry, the ability to absorb water, the rate of this absorption, and breakdown mechanism.

Selection Criteria of Polymer :

- The polymers should have regulatory approval.
- It may have proper drug-polymer interaction.
- The polymers should easily biodegradable.
- The polymers should have greater penetration power.
- Simple mechanism of degradation yielding no toxic monomer residue.
- Properties like bulk hydrophilicity, morphology, structure, and extent of drug polymer interactions can be manipulated by adding copolymer in different ratio.[5]

Safety Evaluation of a Microneedle Prototype in the Gastrointestinal Tract

The safety and ability for natural passage of a microneedle-containing device via the GI tract was investigated. Safety and passage time was estimated using the custom-built device. The dimensions of this prototype were modeled

around those of FDA-approved ingestible devices, such as the video capsule endoscope. The microneedles were placed radially around the device to ensure maximal apposition of the needles with the GI mucosa. A metal core was added to aid in the visualization of the pill on radiographs. The device was endoscopically deployed in the stomach of three animals. The animals were monitored daily and radiographs were taken to track the pill movement and to monitor for any evidence of intestinal obstruction or perforation. Throughout the transit time of the prototype, all animals remained free of clinical signs of obstruction. Furthermore, radiographs remained free of evidence of intestinal obstruction or perforation. Loss of a detectable radiopaque device on the radiographs was used to determine the approximate transit time of the prototypes. The passage time of the device in three different animals was 7, 19, and 56 days. Upon loss of the radiopaque device, the animals were euthanized, and the entire GI tract was examined and found to be macroscopically normal. Further, the three sites of constriction in the GI tract distal to the site of prototype deployment (pylorus, ileocecal valve, and anal canal) were examined and appeared normal. Additionally, these three points were also fixed in formalin for histological examination . Histological examination was notable for normal appearing tissue at all three sites of constriction in the GI tract in the three animals.

Drug release Mechanism from Polymer

Biodegradation and erosion is that the main mechanism of drug unharness. Degradation is characterised by a loss of mass and initiates compound erosion. Polymer degradation in the course of modification within the properties like enduringness, color, shape etc. of a polymer or polymer based product under the influence of one or more environmental factors such as heat, light or chemicals.[9] The polymer degradation can be classified as follows:-

a. Physical erosion
b. Chemical erosion

A. Physical Erosion:

The physical erosion mechanisms are often categorised as heterogeneous or homogenised. In heterogeneous erosion, also called as surface erosion, the polymer erodes only at the surface, and maintains its physical integrity as it degrades. Most polymers undergo homogeneous erosion, means the hydrolysis happens at even rate throughout the compound matrix. Generally these polymers tend to be additional hydrophilic than those exhibiting surface erosion. As a result, water penetrates the polymeric matrix and increases the rate of diffusion. In homogenised erosion, there's loss of integrity of the compound matrix.[3]

B. Chemical Erosion:

Many mechanisms exist for chemical degradation such as mechanism I, II or III. In mechanism I the water-soluble macromolecules that are cross-linked are prone for degradation to form three-dimensional network. In Mechanism II the dissolution of water-insoluble macromolecules with aspect groups that unit of measurement converted to soluble polymers happens as a results of ionization, protonation or reaction of the groups. Materials displaying type II erosion embrace ester derivatives and half esterified copolymers of maleic compound. These polymers become soluble by ionization of cluster} group. Mechanism III is followed by the insoluble polymers with labile bonds. reaction of labile bonds causes cutting of the matter backbone, thereby forming Mass, soluble molecules. Polymers undergoing type III erosion embrace poly (lactic acid), poly (glycolic acid) and their copolymers, poly (ortho esters), polyamides, poly (alkyl-2-cyanoacrylates) and polyanhydrides. typically the three mechanisms are not reciprocally exclusive; mixtures of them can occur throughout drug delivery methodology.[6]

Methods of learning matter Degradation:

1. Morphological changes (swelling, deformation, bubbling, disappearance…)
2. Weight lose
3. Thermal behavior changes
4. Differential Scanning activity (DSC)
5. Mass changes
6. Dilute resolution body
7. Size exclusion chromatography(SEC)
8. Gel permeation chromatography(GPC)
9. MALDI spectroscopy modification in chemistry
10. Infared spectrometry (IR)
11. Resonance spectrometry (NMR)[9]

Application of Biodegradable pills:

- Biodegradable pills unit of measurement accustomed treat gut and abdomen connected diseases or disorder.

- Biodegradable pills unit of measurement be taken orally instead of taking injection.
- It is extraordinarily convenient dose kind for specific drug delivery system.
- The microneedles successfully injected endocrine into the liner of the abdomen, bowel, and colon, inflicting the animals' glucose levels to drop.[9]

3. CONCLUSION:

Biodegradable pills unit of measurement novel approach which can be incorporated with inside the fashion of perishable capsule or inside the fashion of array are observed as a attainable carrier for the delivery of varied molecule medication for the effective oral drug delivery. These painless systems unit of measurement slowly gaining importance and would qualify to be one in all the mandatory devices for controlled drug unleash in future. thus it had been terminated that, these systems represented it to be Associate in Nursing snug and superior carriers as compared to different needle primarily based formulation for the body covering delivery.

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REFERENCES

1. Kotta kranti kumar, V B Reddy *Biodegradable polymers and their role in drug delivery* .14-16
2. Dr.A. Sambasivarao, M.H.Reddy *" A role of biodegradable polymers in controlled drug delivery systems and It's application-A Review* (2017) by Journal of Scientific Research in Pharmacy.
3. Peter J. Tarcha and R..S. Levinson *"Polymers for Controlled Drug Delivery*" CRC PRESS by Special Indian Edition second Indian reprint; 2013 pg no 269-270
4. Babak Ghanbarzadeh and Hadi Almasi *Biodegradable Polymers.* Chapter 6
5. Aggarwal S, Goel A, Singla S: *Drug Delivery: Special Emphasis Given On Biodegradable Polymers Advances In Polymer Science And Technology*,An International Journal, 2012; 2 (1): 1-15
6. Giovanni Traversoa,b,c,1, Carl M. Schoellhammerb,c,1, Avi Schroederc,d,1, Ruby Maab, Gregory Y. Lauwerse, Baris E. Polatb,c, Daniel G. Andersonb,c,f,g,2, Daniel Blankschteinb,2, and Robert Langer "*Microneedles for Drug Delivery via the Gastrointestinal Tract"*
7. *Synthetic Biodegradable Polymers Used in Controlled Drug Delivery System: An Overview* Amit Jagannath Gavasane1 and Harshal Ashok Pawar
8. *Technical advancement in biodegradable polymers and their recent patents* t. Phale*, j. Agnihotri, a.khale
9. Sabir MI,XuX & Li L:A *Review On Biodegradable Polymeric Materials For Bone Tissue Engineering Applications,* J Mater Sci.2009; 44:5713–5724
10. VromanI And Tighzert L:*Biodegradable Polymers, Materials*2009, 2: 307-344