ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/25oct646

Biodegradable Implants and In-Situ Forming Systems: Advances in Sustained and Localized Drug Delivery

Chaitanya Dixit Dornala[1*]; Keerthi G.[2]; Sri Ramchandra Magam[3]; Hania Zainab Bhatti[4]

[1]Department of Pharmaceutical Analysis, Dr. K.V. Subba Reddy Institute of Pharmacy, Dupadu Kurnool-518218, Andhra Pradesh, India
[2]Final Year B. Pharm Student, Dr. K.V. Subba Reddy Institute of Pharmacy, Dupadu, Kurnool-518218, Andhra Pradesh, India.
[3]Department of Pharmacology, Dr. K.V. Subba Reddy Institute of Pharmacy, Dupadu Kurnool-518218, Andhra Pradesh, India.
[4]Final Year B. Pharm Student, Dr. K.V. Subba Reddy Institute of Pharmacy, Dupadu, Kurnool-518218, Andhra Pradesh, India.

Corresponding Author: Chaitanya Dixit Dornala[1*]

Publication Date: 2025/10/25

Abstract: Biodegradable implants and in-situ gels are transforming drug delivery by enabling precise, localized, and sustained release of medications while naturally breaking down into harmless byproducts in the body. Unlike traditional treatments requiring frequent dosing or invasive removal surgeries, these systems improve patient comfort and adherence by reducing side effects and minimizing procedural risks. Biodegradable implants are compact devices, often inserted through minimally invasive methods, designed to deliver drugs or support tissue healing over extended periods. In-situ gels start as liquids and rapidly transition to gels in response to body temperature, pH, or other triggers, ensuring that drugs remain at the target site longer for improved effectiveness. Recent advancements in smart polymers, biosensing technology, and innovative manufacturing methods such as 3D and 4D printing are enabling highly personalized and adaptive therapies tailored to individual patients. The incorporation of nanotechnology further enhances these platforms by improving drug targeting, tissue integration, and controlled responsiveness to physiological signals. These technologies have made significant clinical strides across oncology, ophthalmology, orthopaedics', cardiovascular medicine, and nerve repair. However, challenges remain in fine-tuning degradation rates, ensuring mechanical stability, achieving consistent formulation performance, and meeting stringent regulatory requirements. Addressing these issues through interdisciplinary collaboration and rigorous evaluation is crucial for their widespread clinical adoption. Looking ahead, biodegradable implants and in-situ gels are poised to revolutionize personalized medicine by seamlessly combining structural support with smart, site-specific drug delivery. Together, they offer the potential for less invasive, more effective, and patient-centred treatments, improving outcomes and quality of life across diverse medical fields worldwide.

Keywords: *Biodegradable Implants, In-Situ Gels Controlled Drug Delivery, Smart Polymers, Personalized Medicine, Nanotechnology,3D Printing, Sustained Release.*

How to Cite: Chaitanya Dixit Dornala; Keerthi G.; Sri Ramchandra Magam; Hania Zainab Bhatti (2025). Biodegradable Implants and In-Situ Forming Systems: Advances in Sustained and Localized Drug Delivery. *International Journal of Innovative Science and Research Technology*,10(10), 1238-1245. https://doi.org/10.38124/ijisrt/25oct646

I. INTRODUCTION

Biodegradable implants and in-situ gels are advanced drug delivery systems offering sustained, site-specific, and controlled drug release without surgical removal. They degrade into non-toxic byproducts, improving patient compliance by reducing dosing frequency and invasiveness.[1]

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/25oct646

II. KEY CONCEPTS

Biodegradable Implants: Compact, sterile devices inserted via minimally invasive methods for local or systemic drug delivery. Polyester-based implants are widely used due to their safety record.[2]

- *In-Situ Gels ("Smart Hydrogels"):*

Liquid formulations transforming into gels inside the body via physiological triggers (temperature, pH). They prolong drug retention, enable bio adhesion, and support sustained release.[3]

- *Degradation:*

Occurs through biodegradation (chemical/enzymatic breakdown) and bioerosion (polymer matrix dissolution). Polymer choice dictates release rate, duration, and safety.[4]

- *Recent Developments:*

Smart polymers, 3D printing, biosensor integration, and in-situ hardening injectables for real-time monitoring and personalized treatments.[5]

III. LITERATURE REVIEW HIGHLIGHTS

- *4D Bioprinting (Kennedy et al., 2025):*

Enables dynamic, patient-specific implants using shape-memory polymers and hydrogels. Challenges remain in material optimization and regulatory approval.

- *Biodegradable Polymers as Sustainable Alternatives (Dallev et al., 2025):*

Reviews classifications, sources, degradation, and uses of biodegradable polymers, addressing optimization and scaling challenges.[6]

- *Nanotechnology-Based Drug Delivery Systems (Ezike et al., 2024):*

Highlights a shift towards biodegradable platforms improving therapeutic accuracy and targeted distribution.[7]

- *In-Situ Gelling Systems for Ocular Drug Delivery (Ahmed et al., 2024):*

Demonstrates extended drug residence and sustained release, enhancing therapeutic efficacy and patient compliance.[8]

- *In-Situ Gelling Drug Delivery Systems (Vigani et al., 2020):*

Showcases the sol-to-gel transition for ease of administration and prolonged residence time, improving drug release and patient compliance.[9]

- *Environmentally Sensitive Hydrogels (Qui et al., 2012):*

Highlights potential for site-specific drug administration, with ongoing research to improve biocompatibility and responsiveness.

- *PLGA for Drug Delivery and Tissue Engineering (Makadia et al., 2011):*

Emphasizes PLGA's biocompatibility, biodegradability, and FDA approval for controlled release devices.

- *Poly-ε-Caprolactone (PCL) in Drug Delivery (Dash et al., 2012):*

Showcases PCL's use in various formulations for controlled and prolonged drug release.[10]

- *Intraocular Implants (García-Estrada et al., 2021):*

Concludes that biodegradable implants are preferred over non-biodegradable options due to their natural breakdown and lower surgical risks.[11]

IV. BIODEGRADABLE IMPLANTS

- *Core Principles*

- Controlled Biodegradation: Hydrolysis or enzymatic degradation into natural metabolites.
- Sustained Therapeutic Action: Gradual drug release for localized, long-lasting effects.
- No Secondary Surgery: Natural breakdown eliminates surgical removal.[11]

- *Mechanisms of Biodegradation*

- Hydrolytic Degradation: Water molecules cleave polymer bonds.
- Enzymatic Degradation: Enzymes hasten polymer breakdown.
- Oxidative Degradation: Reactive oxygen species damage implants.[12]

- *Biodegradable Polymer Types*

- Natural Polymers:
- Polysaccharides (alginate, chitosan, cellulose, starch)
- Proteins (silk fibroin, collagen, gelatin)
- Natural polyesters (PHA, poly(3-hydroxybutyrate))[13]
- Synthetic Polymers:
- Aliphatic polyesters (PLA, PGA, PCL, PLGA)
- Polyamides (Nylon-2, Nylon-4)
- Poly(anhydrides)
- Poly (Ortho esters) [14]

- *Semi-Synthetic Polymers*

✓ Cellulose derivatives (carboxymethyl cellulose, cellulose acetate)
✓ Starch blends (starch-PCL) [15]

- *Implications for Drug Delivery and Healing*

- Controlled Drug Release: Polymer properties modulate diffusion and erosion, controlling release kinetics.
- Tissue Integration: Polymer resorption replaced by new tissue growth.[16]

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/25oct646

➢ *Applications*

- Orthopaedics: Fracture fixation, ligament reconstruction, bone scaffolds.
- Oral Health: Guided bone regeneration, dental scaffolds, and screws.
- Cardiovascular: Bioresorbable stents, clips, and sutures.[17]
- Neurosurgery: Dura mater repair, drug delivery for brain malignancies.
- Regenerative Medicine: Tissue growth scaffolds, stem cell delivery.
- Ophthalmology: Drug-eluting implants for glaucoma or uveitis.[18]

➢ *Advantages*

- No removal operation required.
- Decreased long-term complications.
- Better biocompatibility.[19]

V. FACTORS AFFECTING BIODEGRADABLE IMPLANTS

➢ Material Composition/Chemistry: Polymer or metal type determines degradation products and rate. Geometry, Surface Area.
➢ Morphology: Shape, size, porosity, and surface features influence degradation speed.[20]
➢ Surface Chemistry and Coatings: Treatments modulate corrosion/degradation and immune responses.
➢ Mechanical Load/Stress Environment: Stresses accelerate degradation; matching tissue properties is crucial.[21]
➢ Local Environment in the Body: pH, chloride concentration, fluid flow, and biological milieu affect degradation.
➢ Degradation Product Toxicity/Biocompatibility: Released products must be non-toxic and safely cleared.[23]
➢ Rate of Degradation vs. Tissue Healing: Implant integrity must last until tissue can bear the load.
➢ Sterilization and Manufacturing Process: Methods can introduce defects altering degradation.[24]
➢ Host Response/Immune Reactions: Foreign body reaction influences implant success.
➢ Location of Implantation: Different tissues offer varying conditions affecting degradation.[25]

VI. REGULATORY ASPECTS OF BIODEGRADABLE IMPLANTS

➢ Product Classification: Typically, Class IIb or III (EU MDR); requires 510(k) or PMA (FDA).
➢ Standards & Testing: Biocompatibility (ISO 10993), degradation, mechanical performance, sterility (ISO 13485).[26]
➢ Regulatory Pathways: FDA (preclinical/clinical data, IDE, PMA/510(k)); EU (CE mark, Notified Body, clinical evaluation).
➢ Material & Degradation Byproducts: By-products must be non-toxic and safely excreted (ISO 10993-9, -13).
➢ Clinical Data & Performance: Preclinical and clinical trials to show safety and efficacy.[27]
➢ Quality Management & Manufacturing: ISO 13485 for reproducibility, traceability, and cleanliness.
➢ Post-Market Surveillance: Tracking adverse events and long-term follow-up.[28]
➢ Labelling, Instructions, Use: Describe degradation, implantation, and contraindications.

VII. MARKETED/APPROVED BIODEGRADABLE IMPLANTS

➢ Intraocular Sustained-Release Implants: Retisert, Iluvien, Ozurdex.

- Orthopedic/Trauma Devices (Inion Ltd.): Screws, pins, plates using PLA, PGA.
- Biodegradable Polymer Drug-Eluting Stents: Similar efficacy/safety to durable polymer DES.[30]
- Bioresorbable Metal Implants: RemeOs trauma screw (Bioretec Ltd.).
- Other Materials: PLA, PGA, PLGA, PCL, ceramics, bioactive glasses.[31]

➢ *Pipeline/Research/Clinical Trials*

- 3D-Printed Breast Implants: Clinical trial (NCT06993714) evaluating reconstruction.
- Biodegradable Metals: Research into Mg, Zn, Fe alloys.
- Composite Polymeric Implants: High mechanical strength.[32]
- Evonik's Composites: Polymer composites for internal fixation.
- Coatings: Hydrophilic coatings for biocompatibility.
- Tunable Implants: Poly (propylene carbonate)-starch composites.[33]

VIII. CHALLENGES & CONSIDERATIONS

➢ Mechanical strength in load-bearing settings.
➢ Controlling degradation rate and byproduct toxicity.[34]
➢ Regulatory approvals.
➢ Imaging visibility.[35]

IX. IN-SITU GELS

Drug delivery methods that transform from liquids to gels inside the body, allowing localized and prolonged drug release.[36]

➢ *Types of In-Situ Gels*

- Thermally Triggered: Gel formation via temperature changes (PNIPAAm, Pluronic F-127).
- pH-Triggered: Gel formation via pH shifts (polyacrylate, carbopol, alginate).
- Ion-Activated: Gelation triggered by ionic interactions (gellan gum, alginate, gelatin).[37]
- Enzyme-Triggered: Enzyme cleavage causes gelation.
- Multi-Responsive: Respond to multiple stimuli.[38]

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/25oct646

➢ *Mechanisms of In-Situ Gels*

- *Physical Mechanisms:*

✓ Swelling: Polymer absorbs water and expands.
✓ Diffusion: Solvent diffusion causes polymer coagulation.
✓ Physiological Stimuli-Triggered Mechanisms:[39]
✓ Temperature-Sensitive: Sol-gel transition at critical temperature (PNIPAAm).
✓ pH-Triggered: Polymers react to pH changes (polyacrylates, alginates).
✓ Ion-Activated: Ions trigger polymer crosslinking (Ca2+, Mg2+, Na^{+}).[40]

- *Chemical Mechanisms:*
  Enzymatic reactions, photo-initiated polymerization.

➢ *Drug Release Mechanisms*

- Diffusion-Controlled: Drug diffuses through the gel matrix.
- Erosion-Controlled: Gel matrix erodes over time.[41]
- Swelling-Controlled: Polymer swells, controlling drug diffusion.
- Stimuli-Responsive: Triggers cause changes in gel structure.
- Combination Mechanisms: Diffusion + erosion.[42]

➢ *Polymer Types*

- Natural Polymers: Alginic acid, carrageenan, chitosan, guar gum, gellan gum, pectin, sodium hyaluronate, xanthan gum, xyloglucan.
- Synthetic/Semi-Synthetic Polymers: Cellulose acetate phthalate, hydroxypropyl methylcellulose, methylcellulose, polyacrylic acid, PLGA, poloxamers.[43]

➢ *Routes of Administration:*
Ocular - Oral - Nasal - Buccal - Rectal - Vaginal - Injectable (Parenteral) - Intravenous - Intraperitoneal - Intravesical – Cervical.

➢ *Advantages*

- No removal surgery.
- Decreased long-term complications.
- Better biocompatibility.

➢ *Limitations*

- Lower mechanical strength than metals.
- Controlling degradation process.
- Acidic byproducts.
- Higher costs.
- Difficult intervention after implantation.[44]

X. COMBINATION SYSTEMS

➢ *Implants with In-Situ Gel Coatings*

- Polymeric Coatings: PLGA, PCL for controlled breakdown and drug release.
- Hydrogel Coatings: Gelatin, chitosan, alginate (natural); PEG, PAA, PNIPAm (synthetic).
- Ceramic Coatings: Hydroxyapatite (HA) for bone integration.
- Drug-Eluting Coatings: Sirolimus-coated stents.
- Coatings in In-Situ Gels: Mucoadhesive, enteric, stimuli-responsive, protective coatings.

➢ *Synergistic Benefits*
Greater therapeutic efficacy, lower systemic toxicity, longer drug release, improved patient compliance, and tailored administration.[45]

➢ *Recent Advances and Case Studies*

- Cancer Therapy: Intratumoral delivery of paclitaxel (poloxamer-based gels), doxorubicin (chitosan-poloxamer implants), copper-selenium nanoparticles (PLGA-PDMS implants).
- Ocular Applications: Thermo-responsive and ion-activated gels, nanoparticle-loaded gels.
- Bone Regeneration: Methylcellulose-based hydrogels, alginate, and gellan gum gels.

➢ *Nanotechnology Integration*

- Nanoparticles, nanofibers, nanogels enhance biological and mechanical performance.
- Polymeric Nanoparticles: PLGA, chitosan, PEG for drug encapsulation.
- Lipid-Based Carriers: Liposomes for hydrophobic drugs.
- Nanohydroxyapatite (nHA): Bone bonding and mineralization.
- Nanofibers: ECM-like structures for cell attachment.
- Nanogels: Triggered and targeted drug release.
- Metal Nanoparticles: Antimicrobial or imaging-enhancing properties.[46]

XI. BIODEGRADABLE IMPLANTS IN PERSONALIZED MEDICINE

➢ *Personalization Through 3D Printing*
Individualized implants printed to fit unique anatomical structures.

➢ *The Leap to 4D Bioprinting*
Implants adapt dynamically to the patient's physiological environment.

➢ *In-Situ Gels for Tailored Drug Delivery*
Personalized formulations tuned for tumour therapy, chronic inflammation, or neurological conditions.[47]

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/25oct646

➢ *Advances in Internal Medicine Applications*

- Cardiovascular: Biodegradable stents and pacing devices.
- Vascular Tissue Engineering: Stents restore vessel patency.
- Nerve Repair: Conduits and scaffolds for axonal regeneration.

XII. CHALLENGES IN CLINICAL TRANSLATION

➢ *Challenges with Biodegradable Implants*

- Controlling degradation rate and behavior.
- Interaction with body fluids.
- Need for mechanical strength and stability.
- Uncertainties around biosafety.

➢ *Challenges with In-Situ Gels*

- Formulation difficulties.
- Drug stability and bioavailability.
- Stability and shelf-life.

XIII. REGULATORY CONSIDERATIONS

➢ *Regulatory Pathways for Biodegradable Implants*

- In vitro evaluations (ISO 10993).
- In vivo preclinical studies.
- Phase I-III clinical trials.
- ISO 13485 compliance.
- Post-market surveillance.[48]

XIV. EVALUATION AND CHARACTERIZATIONS OF IN SITU GEL SYSTEM

➢ Clarity
➢ Texture analysis
➢ Sol-Gel transition temperature and gelling time
➢ Gel-Strength
➢ Viscosity and rheology

XV. SAFETY AND REGULATORY ASPECTS OF IN-SITU GELS

➢ Gelation process reliability.
➢ Stability and biocompatibility.
➢ Controlled drug release profiles.
➢ Non-toxic metabolites.[49]

- *Common Safety Considerations*

✓ Avoidance of toxic degradation byproducts.
✓ Minimization of immune/inflammatory responses.
✓ Thorough material characterization.
✓ Long-term studies.
✓ Environmental implications.

- *Safety Considerations Common to Both Systems*

✓ Avoidance of toxic degradation byproducts.
✓ Minimization of inflammatory and immune responses.
✓ Thorough characterization of polymer materials and additives.
✓ Long-term studies to understand chronic effects and biodegradation kinetics.
✓ Environmental considerations of polymer sourcing and degradation products.[50]

XVI. CONCLUSION

Biodegradable implants and in-situ gels represent a paradigm shift in drug delivery and regenerative medicine, offering controlled, localized, and sustained therapeutic release. Nanotechnology integration amplifies their potential, enabling precision drug targeting and improved tissue integration. Continued innovation and rigorous evaluation are essential for routine clinical adoption, paving the way for personalized, minimally invasive, and highly effective treatments.

REFERENCES

[1]. Dash, T. K., & Konkimalla, V. B. (2012). Poly-ϵ-caprolactone based formulations for drug delivery and tissue engineering: A review. Journal of Controlled Release, 158(1), 15–33. https://doi.org/10.1016/j.jconrel.2011.09.064

[2]. Mujahidul islam', Indian scientist dr Hemachandran Ravikumar. Orlean college of pharmacy, macy, knowledge park, gressier moika up Reval Royal s society of biology, UK international Journal of Pharmaceutical Research and Applications INNN: 2456-4494 Volume 10, Issue 3 May-June 2025, pp: 2271-2276 www.ijprajournal.com DOI: 10.35629/4494-100322712276 Impact Factor value 7.429 ISO 9001: 2008 Certified Jounal Page 2271.

[3]. Tsung TH, Chen YH, Lu DW. Updates on Biodegradable Formulations for Ocular Drug Delivery.Pharmaceutics.2023 Feb 22;15(3):734. doi: 10.3390/pharmaceutics15030734. PMID: 36986595; PMCID: PMC10057390.: 10.3390/pharmaceutics15030734

[4]. Holcman V, Dallaev R, Papež N, Allaham MM. Biodegradable Polymers: Characteristics, Uses, and Environmental Effects. Basel polymers. July 18, 2025, 17(14):1981. 10.3390/polym17141981 is the doi. PMCID: PMC12298952; PMID: 40732859.

[5]. A Review on Advanced Drug Delivery Systems Using 3D-Printed Biodegradable Polymers: Review Article. (2025). Journal of Pharma Insights and Research, 3(3), 127-140. https://doi.org/10.69613/2q6qdy97.

[6]. Heying R, Mela P, Mozafari M, and Kabirian F. Biodegradable 3D-printed cardiovascular implants function better when controlled release systems are used. doi: 10.1021/acsbiomaterials.3c00559. Epub 2023 Oct 19. PMID: 37856240. ACS Biomater Sci Eng. 2023 Nov 13;9(11):5953-5967.

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/25oct646

[7]. Picco CJ, Domínguez-Robles J, Utomo E, Paredes AJ, Volpe-Zanutto F, Malinova D, Donnelly RF, Larrañeta E. 3D-printed implantable devices with biodegradable rate-controlling membrane for sustained delivery of hydrophobic drugs. Drug Deliv. 2022 Dec;29(1):1038-1048. doi: 10.1080/10717544.2022.2057620. PMID: 35363100; PMCID: PMC8979538.

[8]. Middleton, J. C., & Tipton, A. J. (2000). Synthetic biodegradable polymers as orthopedic devices. Biomaterials, 21(23), 2335–2346. https://doi.org/10.1016/S0142-9612(00)00101-0.

[9]. Xia B, Liu Y, Xing Y, Shi Z, Pan X. Biodegradable Medical Implants: Reshaping Future Medical Practice. Adv Sci (Weinh). 2025 Sep;12(35): e08014. doi: 10.1002/advs.202508014. Epub 2025 Aug 9. PMID: 40782070; PMCID: PMC12462970.

[10]. Hydrolytic Degradation and Erosion of Polyester Biomaterials Lindsay N. Woodard and Melissa A. Grunlan ACS Macro Letters 2018 7 (8), 976-982 DOI: 10.1021/acsmacrolett.8b00424

[11]. 11.Li Y, Chen Q, Shi H, and Thouas GA have conducted a study on the breakdown of poly (polyol sebacate) by oxidation and enzymes. The DOI for the article published in April 2014 in the Journal of Biomaterials Applications, volume 28, issue 8, pages 1138-50 is 10.1177/0885328213499195. July 31, 2013. PMID: 23904286. Epub.

[12]. Li Y, Chen Q, Shi H, and Thouas GA have conducted a study on the breakdown of poly (polyol sebacate) by oxidation and enzymes. The DOI for the article published in April 2014 in the Journal of Biomaterials Applications, volume 28, issue 8, pages 1138-50 is 10.1177/0885328213499195. July 31, 2013. PMID: 23904286. Epub.

[13]. Sudesh, K., Abe, H., Doi, Y. (2000). Synthesis, structure and properties of polyhydroxyalkanoates: biological polyesters. Progress in Polymer Science, 25(10), 1503–1555. https://doi.org/10.1016/S0079-6700(00)00035-6.

[14]. Dash, T. K., & Konkimalla, V. B. (2012). Poly-ϵ-caprolactone based formulations for drug delivery and tissue engineering: A review. Journal of Controlled Release, 158(1), 15–33. https://doi.org/10.1016/j.jconrel.2011.09.064.

[15]. Thakur, V.K., Thakur, M.K. (2014). Processing and characterization of natural cellulose fibers/thermoset polymer composites. Carbohydrate Polymers, 109, 102–117. https://doi.org/10.1016/j.carbpol.2014.03.039.

[16]. Athanasiou KA, Singhal AR, Agrawal CM, Boyan BD. In vitro degradation and release characteristics of biodegradable implants containing trypsin inhibitor. Clin Orthop Relat Res. 1995 Jun;(315):272-81. PMID: 7634681.

[17]. Hydrolytic Degradation and Erosion of Polyester Biomaterials Lindsay N. Woodard and Melissa A. Grunlan ACS Macro Letters 2018 7 (8), 976-982 DOI: 10.1021/acsmacrolett.8b00424

[18]. Humberto Valencia C. Hydrolytic degradation and in vivo resorption of poly-l-lactic acid-chitosan biomedical devices in the parietal bones of Wistar rats. Journal of International Medical Research. 2019;47(4):1705-1716. doi:10.1177/0300060519828935

[19]. Kotteda AK, Saikumar T, Shreegan AA. Advancements in Biodegradable Orthopaedic Implants: A Literature Review. Indian J Orthop. 2025 Jun 22;59(8):1090-1100. doi: 10.1007/s43465-025-01445-y. PMID: 40852561; PMCID: PMC12367625.

[20]. Thakur, V.K., Thakur, M.K. (2014). Processing and characterization of natural cellulose fibers/thermoset polymer composites. Carbohydrate Polymers, 109, 102–117. https://doi.org/10.1016/j.carbpol.2014.03.039.

[21]. Amini AR, Wallace JS, Nukavarapu SP. Short-term and long-term effects of orthopedic biodegradable implants. J Long Term Eff Med Implants. 2011;21(2):93-122. doi: 10.1615/jlongtermeffmedimplants. v21.i2.10. PMID: 22043969; PMCID: PMC3470866.

[22]. Huang C, Yang H, Shi J, He W, Zheng Y, Chen S, Lu Y, Zhang T, Chen K, Canavese F. Biodegradable metals are replacing absorbable polymers in the use of biodegradable implants in pediatric orthopedics. PMID: 40256329; PMCID: PMC12008652; doi: 10.1016/j.bioactmat.2025.04.001. Bioact Mater. 2025 Apr 10; 50:189-214.

[23]. Huang C, Yang H, Shi J, He W, Zheng Y, Chen S, Lu Y, Zhang T, Chen K, Canavese F. Biodegradable metals are replacing absorbable polymers in the use of biodegradable implants in pediatric orthopedics. PMID: 40256329; PMCID: PMC12008652; doi: 10.1016/j.bioactmat.2025.04.001. Bioact Mater. 2025 Apr 10; 50:189-214.

[24]. Amini AR, Wallace JS, Nukavarapu SP. Short-term and long-term effects of orthopedic biodegradable implants. J Long Term Eff Med Implants. 2011;21(2):93-122. doi: 10.1615/jlongtermeffmedimplants. v21.i2.10. PMID: 22043969; PMCID: PMC3470866.

[25]. Amini AR, Wallace JS, Nukavarapu SP. Short-term and long-term effects of orthopedic biodegradable implants. J Long Term Eff Med Implants. 2011;21(2):93-122. doi: 10.1615/jlongtermeffmedimplants. v21.i2.10. PMID: 22043969; PMCID: PMC3470866.

[26]. Seetharaman S, Gupta M, and Sankaranarayanan D. Magnesium-Based Temporary Implants: Prospects, Present Situation, Uses, and Difficulties. Biomater J Funct. June 17, 2023; 14(6):324. 10.3390/jfb14060324 is the doi. PMCID: PMC10299300; PMID: 37367288.

[27]. Huang C, Yang H, Shi J, He W, Zheng Y, Chen S, Lu Y, Zhang T, Chen K, Canavese F. Biodegradable metals are replacing absorbable polymers in the use of biodegradable implants in pediatric orthopedics. PMID: 40256329; PMCID: PMC12008652; doi: 10.1016/j.bioactmat.2025.04.001. Bioact Mater. 2025 Apr 10; 50:189-214.

[28]. B. Xia, Y. Liu, Y. Xing, Z. Shi, and X. Pan, "Biodegradable Medical Implants: Reshaping Future Medical Practice." Adv. Sci. 12, no. 35 (2025): 12, e08014. https://doi.org/10.1002/advs.202508014.

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/25oct646

[29]. Huang C, Yang H, Shi J, He W, Zheng Y, Chen S, Lu Y, Zhang T, Chen K, Canavese F. Biodegradable metals are replacing absorbable polymers in the use of biodegradable implants in pediatric orthopedics. PMID: 40256329; PMCID: PMC12008652; doi: 10.1016/j.bioactmat.2025.04.001. Bioact Mater. 2025 Apr 10; 50:189-214.

[30]. Recent advances in bio-medical implants; mechanical properties, surface modifications and applications Mohammed Zwawi Engineering Research Express, Volume 4, Number 3 Mohammed Zwawi 2022 Eng. Res. Express 4 032003DOI 10.1088/2631-8695/ac8ae2

[31]. Amini AR, Wallace JS, Nukavarapu SP. Short-term and long-term effects of orthopedic biodegradable implants. J Long Term Eff Med Implants. 2011;21(2):93-122. doi: 10.1615/jlongtermeffmedimplants. v21.i2.10. PMID: 22043969; PMCID: PMC3470866.

[32]. Amini AR, Wallace JS, Nukavarapu SP. Short-term and long-term effects of orthopedic biodegradable implants. J Long Term Eff Med Implants. 2011;21(2):93-122. doi: 10.1615/jlongtermeffmedimplants. v21.i2.10. PMID: 22043969; PMCID: PMC3470866.

[33]. Huang C, Yang H, Shi J, He W, Zheng Y, Chen S, Lu Y, Zhang T, Chen K, Canavese F. Biodegradable metals are replacing absorbable polymers in the use of biodegradable implants in pediatric orthopedics. PMID: 40256329; PMCID: PMC12008652; doi: 10.1016/j.bioactmat.2025.04.001. Bioact Mater. 2025 Apr 10; 50:189-214.

[34]. Wang L, Guo X, Chen J, Zhen Z, Cao B, Wan W, Dou Y, Pan H, Xu F, Zhang Z, Wang J, Li D, Guo Q, Jiang Q, Du Y, Yu J, Heng BC, Han Q, Ge Z. Key considerations on the development of biodegradable biomaterials for clinical translation of medical devices: With cartilage repair products as an example. Bioact Mater. 2021 Aug 3; 9:332-342. doi: 10.1016/j.bioactmat.2021.07.031. PMID: 34820574; PMCID: PMC8586440.

[35]. Wang L, Guo X, Chen J, Zhen Z, Cao B, Wan W, Dou Y, Pan H, Xu F, Zhang Z, Wang J, Li D, Guo Q, Jiang Q, Du Y, Yu J, Heng BC, Han Q, Ge Z. Key considerations on the development of biodegradable biomaterials for clinical translation of medical devices: With cartilage repair products as an example. Bioact Mater. 2021 Aug 3; 9:332-342. doi: 10.1016/j.bioactmat.2021.07.031. PMID: 34820574; PMCID: PMC8586440.

[36]. Aikin, Mykyta, Vadim Shalomeev, Volodymyr Kukhar, Andrii Kostryzhev, Ihor Kuziev, Viktoriia Kulynych, Oleksandr Dykha, Volodymyr Dytyniuk, Oleksandr Shapoval, Alvydas Zagorskis, and et al. 2025. "Recent Advances in Biodegradable Magnesium Alloys for Medical Implants: Evolution, Innovations, and Clinical Translation" Crystals 15, no. 8: 671. https://doi.org/10.3390/cryst15080671

[37]. Wang L, Guo X, Chen J, Zhen Z, Cao B, Wan W, Dou Y, Pan H, Xu F, Zhang Z, Wang J, Li D, Guo Q, Jiang Q, Du Y, Yu J, Heng BC, Han Q, Ge Z. Key considerations on the development of biodegradable biomaterials for clinical translation of medical devices: With cartilage repair products as an example. Bioact Mater. 2021 Aug 3; 9:332-342. doi: 10.1016/j.bioactmat.2021.07.031. PMID: 34820574; PMCID: PMC8586440.

[38]. Dykha, O., Dytyniuk, V., Shapoval, O., Zagorskis, A., Burko, V., Khliestova, O., Titov, V., & Hrushko, O. (2025) Aikin, M., Shalomeev, V., Kukhar, V., Kostryzhev, A., Kuziev, I., Kulynych, V. Current Developments, Innovations, and Clinical Applications of Biodegradable Magnesium Alloys for Medical Implants. 15(8), Crystals, 671. The article is https://doi.org/10.3390/cryst15080671.

[39]. Wang L, Guo X, Chen J, Zhen Z, Cao B, Wan W, Dou Y, Pan H, Xu F, Zhang Z, Wang J, Li D, Guo Q, Jiang Q, Du Y, Yu J, Heng BC, Han Q, Ge Z. Key considerations on the development of biodegradable biomaterials for clinical translation of medical devices: With cartilage repair products as an example. Bioact Mater. 2021 Aug 3; 9:332-342. doi: 10.1016/j.bioactmat.2021.07.031. PMID: 34820574; PMCID: PMC8586440.

[40]. Kotteda AK, Saikumar T, Shreegan AA. Advancements in Biodegradable Orthopaedic Implants: A Literature Review. Indian J Orthop. 2025 Jun 22;59(8):1090-1100. doi: 10.1007/s43465-025-01445-y. PMID: 40852561; PMCID: PMC12367625.

[41]. Wang L, Guo X, Chen J, Zhen Z, Cao B, Wan W, Dou Y, Pan H, Xu F, Zhang Z, Wang J, Li D, Guo Q, Jiang Q, Du Y, Yu J, Heng BC, Han Q, Ge Z. Key considerations on the development of biodegradable biomaterials for clinical translation of medical devices: With cartilage repair products as an example. Bioact Mater. 2021 Aug 3; 9:332-342. doi: 10.1016/j.bioactmat.2021.07.031. PMID: 34820574; PMCID: PMC8586440.

[42]. Wang L, Guo X, Chen J, Zhen Z, Cao B, Wan W, Dou Y, Pan H, Xu F, Zhang Z, Wang J, Li D, Guo Q, Jiang Q, Du Y, Yu J, Heng BC, Han Q, Ge Z. Key considerations on the development of biodegradable biomaterials for clinical translation of medical devices: With cartilage repair products as an example. Bioact Mater. 2021 Aug 3; 9:332-342. doi: 10.1016/j.bioactmat.2021.07.031. PMID: 34820574; PMCID: PMC8586440.

[43]. Tsung TH, Tsai YC, Lee HP, Chen YH, Lu DW. Biodegradable Polymer-Based Drug-Delivery Systems for Ocular Diseases. Int J Mol Sci. 2023 Aug 19;24(16):12976. doi: 10.3390/ijms241612976. PMID: 37629157; PMCID: PMC10455181.

[44]. Thakur R, Jones D, “Biodegradeable Implants for Sustained Intraocular Delivery of Small and Large Molecules”. ON drug Delivery Magazine, Issue 82 (Jan 2018), pp 28-31.

[45]. Kwong JS, Yu CM. Clinical outcomes of biodegradable polymer drug-eluting stents for percutaneous coronary intervention: an updated meta-analysis of randomized controlled trials. Clin Cardiol. 2014 Jul;37(7):440-53. doi: 10.1002/clc.22285. Epub

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/25oct646

2014 Apr 10. PMID: 24723467; PMCID: PMC6649413.

[46]. Kwong JS, Yu CM. Clinical outcomes of biodegradable polymer drug-eluting stents for percutaneous coronary intervention: an updated meta-analysis of randomized controlled trials. Clin Cardiol. 2014 Jul;37(7):440-53. doi: 10.1002/clc.22285. Epub 2014 Apr 10. PMID: 24723467; PMCID: PMC6649413.

[47]. Kyriakides TR, Kim HJ, Zheng C, Harkins L, Tao W, Deschenes E. Foreign body response to synthetic polymer biomaterials and the role of adaptive immunity. Biomed Mater. 2022 Mar 4;17(2):10.1088/1748-605X/ac5574. doi: 10.1088/1748-605X/ac5574. PMID: 35168213; PMCID: PMC9159526.

[48]. Witte F, Calliess T, and Windhagen H. Biodegradable synthetic implants: clinical uses and immunological considerations [Biodegradable artificial implant materials: immunological characteristics and clinical applications]. 2008 Feb. 37(2):125-30; Orthopaedics. PMID: 18214423; German. doi: 10.1007/s00132-008-1193-9.

[49]. Omar R, Saliba W, Khatib M, Zheng Y, Pieters C, Oved H, Silberman E, Zohar O, Hu Z, Kloper V, Broza YY, Dvir T, Grinberg Dana A, Wang Y, Haick H. Biodegradable, Biocompatible, and Implantable Multifunctional Sensing Platform for Cardiac Monitoring. ACS Sens. 2024 Jan 26;9(1):126-138. doi: 10.1021/acssensors.3c01755. Epub 2024 Jan 3. PMID: 38170944; PMCID: PMC10825867.

[50]. Ahsan Riaz Khan, Navdeep Singh Grewal, Chao Zhou, Kunshan Yuan, Hai-Jun Zhang, Zhang Jun, Recent advances in biodegradable metals for implant applications: Exploring in vivo and in vitro responses Results in Engineering, Volume 20,2023,101526, ISSN2590-1230, https://doi.org/10.1016/j.rineng.2023.101526.