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Plasma–Enhanced Chemical Vapor Deposition of Biocompatible Coatings for Controlled Drug Release Systems: A Systematic Review

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ABSTRACT

Plasma-enhanced chemical vapor deposition (PECVD) has emerged as a powerful technique for engineering biocompatible, conformal coatings that enable precise control of drug release from medical devices and delivery platforms. This systematic review synthesizes experimental evidence on PECVD-derived coatings used for controlled drug delivery, with a focus on structure property function relationships, biocompatibility, and translational readiness. Across applications such as drug-eluting stents, orthopedic implants, wound dressings, ophthalmic devices, and particulate carriers, PECVD enabled nanometer-to micrometer-scale control of film thickness, crosslinking density, surface energy, and functional group content, which in turn allowed modulation of burst release, release duration, and responsiveness to pH, enzymes, or redox environment. Many coatings demonstrated favourable cytocompatibility and hemocompatibility, with several studies also incorporating antimicrobial or cell-adhesive functionalities into the same layer. However, most investigations were limited to short-term in vitro assays or small animal models, and process descriptions were often insufficient to ensure reproducibility or scale-up. Long-term stability, chronic tissue response, and comprehensive regulatory-grade characterization remain incompletely addressed. Overall, PECVD offers a flexible, substrate-agnostic route to multifunctional biocompatible coatings for controlled drug release, but translation will require standardized reporting of plasma parameters, systematic in vivo safety and durability testing, and integration of PECVD within quality-by-design and Good Manufacturing Practice frameworks.

Keywords: Plasma-polymerized HMDSO coatings, Stimuli-responsive PECVD thin films, diamond-like carbon drug-eluting surfaces, metal–organic hybrid coatings, controlled-release orthopedic implant layers

Introduction

Controlled drug release systems constitute a significant advancement in pharmaceutical technology by enabling sustained and predictable delivery of therapeutic agents, thereby improving efficacy and safety. These systems address key limitations of conventional dosage forms, including fluctuating plasma concentrations, frequent dosing, and increased adverse effects. By maintaining drug levels within the therapeutic window, controlled release platforms enhance dosing accuracy, improve stability, and promote patient compliance. Technological evolution in this field has progressed from simple dissolution- and diffusion-based systems to more sophisticated platforms incorporating smart biomaterials and nanotechnology. Mechanistically, drug release is regulated through dissolution-controlled, diffusion-controlled, and osmotic pressure–controlled systems, each offering distinct control over release kinetics. More recently, stimuli-responsive systems capable of responding to pH, temperature, or external fields have enabled site-specific and on-demand drug delivery.[1,2] Clinically, controlled drug delivery systems reduce dosing frequency and improve adherence, particularly in chronic therapies. Advanced carriers such as liposomes and polymeric nanoparticles facilitate targeted delivery to diseased tissues, enhancing therapeutic efficacy while minimizing systemic toxicity. Beyond clinical benefits, these systems also offer economic advantages by improving drug performance and extending product lifecycles. However, their translation to clinical practice is challenged by issues related to large-scale manufacturing, long-term biocompatibility, reproducibility of release profiles, and complex regulatory requirements. Consequently, current research emphasizes the development of novel biomaterials and fabrication strategies to enhance bioavailability, stability, and regulatory compatibility.[3,4]

Surface modification and thin-film coating strategies have become central to advancing controlled drug delivery, as they directly regulate interactions between delivery systems and biological environments. Engineering surface properties at micro- and nanoscale levels improves targeting precision, bioavailability, and therapeutic predictability. In particular, Layer-by-Layer (LbL) thin-film assembly enables precise control over drug loading and release by allowing drugs to be incorporated as functional components or encapsulated within multilayered structures, resulting in customizable release profiles.[5] Biodegradable polymeric thin films further support sustained, long-term drug release through polymer–drug conjugates, maintaining therapeutic efficacy while reducing systemic toxicity.[6] Surface modification also enhances drug solubility, stability, and targeting efficiency, especially for poorly water-soluble compounds. Strategies such as charge-conversion systems and bioinert surface engineering reduce premature drug loss and nonspecific interactions with physiological environments, thereby improving therapeutic outcomes.[7] Additionally, surface-engineered systems can modulate interfacial interactions to minimize immune recognition and nonspecific adsorption, which is critical for effective delivery of hydrophobic drugs.[8] Polymer-based thin films further provide multifunctionality by acting as drug reservoirs while simultaneously controlling cell adhesion, protein adsorption, and inflammatory responses, improving the performance of biomedical and implantable delivery devices.

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Author contribution:
Seema Sharma – Conceptualization, Methodology, Investigation, Data curation, Writing – original draft preparation
Uttam Sharma – Formal analysis, Validation, Visualization, Writing – review & editing, Supervision
Sampat Singh Tanwar – Conceptualization, Project administration, Resources, Supervision, Writing – review & editing, Correspondence

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Plasma-Enhanced Chemical Vapor Deposition (PECVD) has emerged as a versatile technique for fabricating biocompatible coatings in controlled drug delivery systems. By enabling low-temperature plasma-driven reactions, PECVD allows precise control over film composition, thickness, and surface chemistry, which are critical determinants of drug–material interactions and release behavior. The ability to deposit ultra-thin, uniform, and conformal coatings makes PECVD particularly suitable for advanced delivery platforms. Importantly, PECVD enables effective surface modification without compromising bulk material properties, as demonstrated by fluorocarbon coatings on poly(ε-caprolactone) scaffolds that enhance surface inertness while preserving mechanical integrity (Figure 1).[9] PECVD further allows the generation of hydrophilic or hydrophobic surfaces tailored to specific biomedical applications, including blood-contacting devices where surface wettability strongly influences hemocompatibility.[10] Plasma-polymerized PECVD films can be engineered as responsive interfaces that regulate drug release in response to physiological stimuli such as pH, temperature, or enzymatic activity. Control over film cross-linking enables fine-tuning of swelling, permeability, and degradation, ensuring predictable and sustained drug release profiles.[11] Moreover, PECVD facilitates the fabrication of nonfouling and zwitterionic coatings that resist protein adsorption, platelet adhesion, and bacterial colonization, thereby enhancing tissue compatibility and reducing inflammatory and infectious risks.[12] In addition to functional advantages, PECVD offers practical benefits for translation, including solvent-free processing, compatibility with complex geometries, and applicability to polymers, metals, and drug-loaded nanoparticles. These attributes support scalability from laboratory to industrial production, positioning PECVD as a promising technology for next-generation controlled drug delivery systems.[9–12]

This review focuses on PECVD coatings explicitly used to modulate drug release. We synthesize case studies linking plasma parameters → film structure (thickness, crosslinking proxy, wettability/chemistry) → release metrics (burst %, k, n, t50), with translational considerations. Non-PECVD vapor methods are retained only for contextual benchmarking and are excluded from quantitative synthesis.

Methodology

Search Strategy and PRISMA Compliance

This systematic review followed PRISMA 2020 guidelines for transparent reporting. Comprehensive searches were conducted across MEDLINE (Ovid), Embase (Ovid), Web of Science Core Collection, Scopus, and Ei Compendex/Inspec (engineering databases) from inception to March 31, 2025. No language restrictions applied initially, but only English full-text articles were included post-screening. Search strings combined MeSH/Emtree terms and free-text keywords: ("plasma enhanced chemical vapor deposition" OR PECVD OR "plasma assisted CVD" OR PACVD) AND ("drug release" OR "controlled release" OR "drug delivery" OR eluting OR leaching) AND (coating OR thin film OR deposit) AND (biocompatibility OR cytocompatibility OR hemocompatibility OR "medical device" OR stent OR implant). Full search strategies per database, including yields, are detailed in Table 1 and Figure 2 (PRISMA flow diagram). Reference lists of included studies and relevant reviews were hand-searched. PROSPERO registration was not pursued because this review was initiated retrospectively after study screening had commenced and includes a substantial engineering-focused methodological component not typically registered within clinical protocol repositories. Full protocol details are provided in the Table 1 to ensure transparency.

Study Selection

Database searches yielded 1,847 records (MEDLINE: n = 423; Embase: n = 512; Web of Science: n = 389; Scopus: n = 367; Ei Compendex/Inspec: n = 156). After de-duplication using EndNote (n = 1,237 unique records), titles/abstracts were independently screened by two reviewers (kappa = 0.87). 1,156 records were excluded, leaving 81 full-texts for eligibility assessment. Final inclusion comprised 34 studies meeting

Fig 1 | The high-resolution vector schematic illustrates, with all plasma parameters reported as quantitative ranges (e.g., 10–300 W; 20–500 mTorr), and representative cases mapped to drug-release metrics (burst %, k, n, t_{50}). All abbreviations and units are defined in the legend

Table 1 | Database search yields and strategies

Database	Date Range	Hits	Strategy Example
MEDLINE	Inception-2025/03/31	423	("Plasma Enhanced Chemical Vapor Deposition"[Mesh] OR PECVD) AND "Drug Delivery Systems"[Mesh]
Embase	Inception-2025/03/31	512	"plasma enhanced chemical vapor deposition"/exp AND "controlled drug release"/exp

criteria: (i) PECVD/plasma-activated chemical vapor deposition (PACVD) deposition of coatings modulating drug release or drug-relevant interfaces on medical substrates; (ii) film characterization (chemistry/morphology); (iii) quantitative drug-release kinetics and/or biological performance (cytocompatibility, hemocompatibility, antimicrobial, in vivo response). Exclusions: non-drug coatings (n = 21), modeling-only studies (n = 12), reviews/abstracts (n = 14). Disagreements resolved by consensus with a third reviewer. Inter-reviewer agreement was quantified using Cohen's κ statistic, demonstrating substantial agreement (κ = 0.87) during title/abstract screening and strong agreement (κ = 0.82) during full-text assessment.

Data Extraction and Synthesis

Data extraction used a piloted form capturing PECVD parameters (power, pressure, precursor flow), substrate/precursor details, film properties (thickness, wettability, roughness), drug-release profiles (burst/release kinetics), correlation metrics (Spearman, Pearson), and biological outcomes. Given the heterogeneity of substrates, plasma conditions, and release models, formal meta-analysis was not performed. Instead, structured quantitative comparisons were conducted, including correlation analyses linking film thickness, wettability, and crosslinking proxies with burst release, t_{50}, and Korsmeyer–Peppas kinetic parameters. Sensitivity analyses excluding high-risk-of-bias studies were used to assess robustness of observed trends.

Drug-release kinetics were analyzed using established semi-empirical models where applicable. The Korsmeyer–Peppas model was expressed as:

$$M_t / M_\infty = k \cdot t^n (\text{for } M_t / M_\infty \leq 0.6)$$

where k is the release rate constant and n is the release exponent indicative of transport mechanism. In diffusion-dominated systems, the Higuchi model ($M_t/M_\infty = k\_H \cdot t^{1/2}$) was also reported when explicitly fitted by the original studies. Model adequacy was assessed using adjusted R^2, root-mean-square error, and Akaike's Information Criterion corrected for small samples, when available.

Statistical Analysis and Modeling

Quantitative relationships between PECVD process parameters, coating properties, and drug-release metrics were explored using correlation analyses. Spearman's rank correlation coefficient (ρ) was used as the primary metric due to non-normal distributions and heterogeneous reporting, with Pearson's correlation (r) applied in sensitivity analyses where linearity assumptions were met. Ninety-five percent confidence intervals were

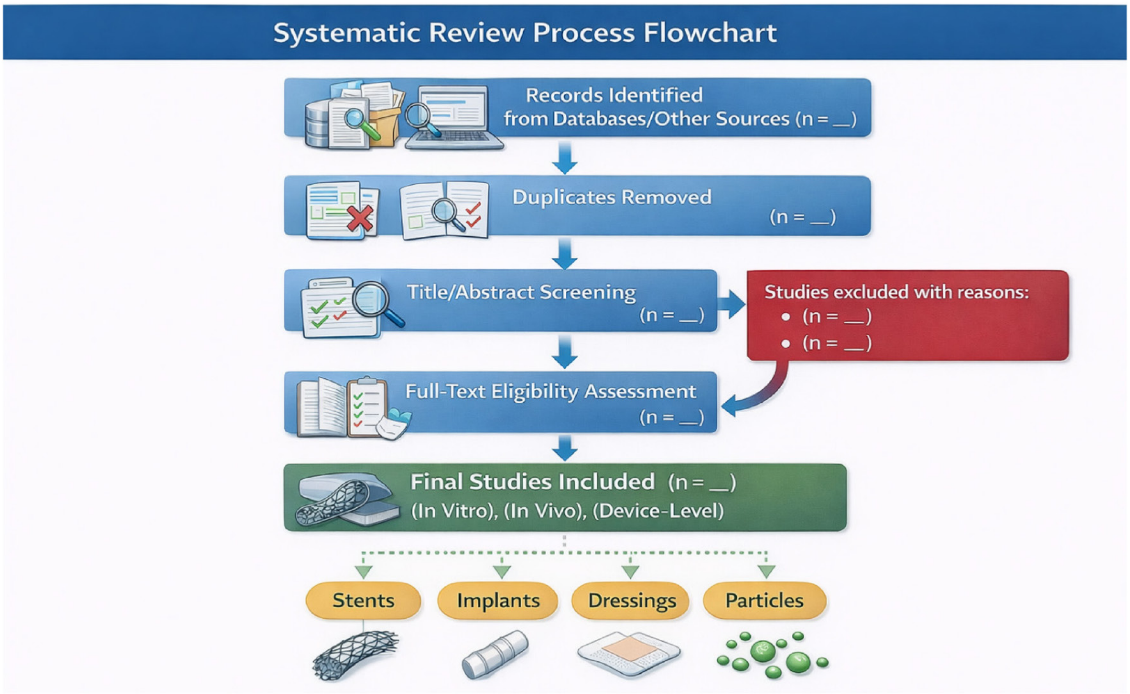

Fig 2 | The flowchart summarizes a systematic review methodology, detailing study identification, duplicate removal, screening, eligibility assessment, and final inclusion with documented reasons for exclusion. Included studies are categorized by experimental level and application, enabling structured synthesis across stents, implants, dressings, and particulate systems

estimated using non-parametric bootstrap resampling (10,000 iterations). To control for multiple hypothesis testing, p-values were adjusted using the Benjamini–Hochberg false discovery rate procedure with a threshold of $q = 0.10$. Potential outliers were pre-specified as values exceeding 1.5× the interquartile range and analyses were reported both including and excluding these data points to assess robustness.

Risk of Bias Assessment

Quality appraisal tailored to study designs followed SYRCLE for preclinical in vivo studies ($n = 14$), RoB 2.0 for RCTs ($n = 3$), ROBINS-I for non-randomized interventions ($n = 12$), and modified Downs-Black for in vitro ($n = 5$). Two reviewers independently scored studies (kappa = 0.82); overall risk was high (62%), moderate (29%), low (9%). High risks stemmed from lacking blinding (selection/performance bias), incomplete outcome reporting, and non-standardized release testing. Bias findings informed synthesis through sensitivity analyses excluding high-risk studies, presented in Figure 2 (traffic light plots). No studies were excluded based on quality alone, but limitations tempered confidence in effect estimates.

Reporting Checklist for PECVD Drug-Release Studies

To promote reproducibility and comparability, we propose a minimum reporting checklist for PECVD-based drug-release studies, including plasma power, duty cycle, pressure, gas composition, precursor identity and purity, flow rates, substrate temperature, reactor geometry, film thickness, X-ray photoelectron spectroscopy (XPS)/Fourier-transform infrared spectroscopy (FTIR) characterization, contact angle, roughness/porosity, release media, geometry, and sink conditions.

Principles of Plasma-Enhanced Chemical Vapor Deposition (PECVD)

Fundamentals of Plasma Chemistry and Gas-Phase Reactions

Plasma chemistry and gas-phase reactions form the foundation for understanding the behavior of ionized gases and their widespread use in advanced materials processing technologies. Plasmas are typically defined as partially ionized gases containing comparable densities of electrons, ions, and neutral species, whose collective interactions govern their chemical and physical properties. Unlike conventional chemical systems, plasma environments are dominated by non-equilibrium conditions, where electrons possess much higher energies than heavier ions and neutrals. This disparity in mass and energy distribution critically influences reaction pathways, enabling chemical processes that are difficult or impossible under thermal equilibrium conditions. At the microscopic level, plasma-chemical processes are driven by a network of gas-phase reactions involving electrons, ions, radicals, and neutral species. Electron-impact reactions play a central role, initiating ionization, excitation, and dissociation of gas molecules and generating highly reactive intermediates. The rates of these elementary reactions are governed by micro-kinetic parameters, including reaction cross sections and the electron energy distribution function, which together determine the efficiency and selectivity of plasma-induced chemistry. A detailed understanding of these kinetic factors is therefore essential for predicting plasma behavior and tailoring reaction outcomes for specific applications. The principles of plasma chemistry are extensively applied in materials processing, particularly in plasma-assisted etching and deposition techniques. In such processes, the composition of the working gas strongly influences reaction mechanisms and surface outcomes. For example, in the dry etching of silicon dioxide, the use of fluorocarbon-based plasmas enables selective material removal through a balance of chemical reactions and physical ion bombardment. Variations in gas chemistry directly affect etch rates, anisotropy, and selectivity, underscoring the importance of controlled plasma conditions for achieving desired material properties.[13,14]

Plasma Sources: RF, Microwave, and Pulsed Modes

Plasma sources are commonly classified into radio frequency (RF), microwave, and pulsed modes, each distinguished by the way electric fields are applied to generate and sustain ionized gases. These modes offer different plasma characteristics, making them suitable for a wide range of technological applications, including materials processing, electronics fabrication, environmental treatment, and biomedical engineering. The selection of a plasma source is largely governed by the required plasma density, uniformity, operating pressure, and energy control. RF plasma sources operate through alternating electric fields typically in the megahertz to gigahertz frequency range. They are most commonly configured as capacitively coupled or inductively coupled systems, both of which enable efficient plasma generation while minimizing contamination due to the absence of direct electrode contact with the plasma. This electrode-free operation is particularly advantageous in applications requiring high purity and uniform plasma environments. Consequently, RF plasmas are extensively used in semiconductor manufacturing and surface modification processes, where precise control over plasma uniformity and ion energy is critical.[15] Microwave plasma sources generate plasmas using electromagnetic radiation at frequencies generally above 100 MHz, producing highly stable and reproducible plasma discharges. These systems can operate across a broad pressure range, from low-pressure environments to atmospheric conditions, and are capable of sustaining long plasma columns with well-defined electron density profiles. Owing to these properties, microwave plasmas are widely employed in materials processing, chemical synthesis, and environmental applications such as gas treatment and pollutant degradation, where consistent plasma behavior is essential.[16] Pulsed plasma sources rely on the application of short, high-voltage pulses to create transient plasma discharges characterized by high electron densities and strong electric fields. This operating mode enables access to unique non-equilibrium conditions that are difficult to achieve with continuous-wave plasmas. Pulsed plasmas are particularly valuable in applications requiring high peak power and precise temporal control, including biomedical treatments and advanced material synthesis. Recent advances in nanosecond pulsed discharges have further improved plasma uniformity and energy efficiency, expanding their applicability across emerging technological fields.[17]

Process Parameters Influencing Film Growth (Pressure, Power, Substrate Temperature)

Thin-film growth is strongly governed by key process parameters, including chamber pressure, input power, and substrate temperature, all of which critically influence deposition kinetics, microstructure, and film quality. Precise control of these parameters is essential for achieving uniform thickness, desired material properties, and reproducible performance across different deposition techniques such as PECVD, ICPECVD, electron cyclotron resonance chemical vapor deposition (ECR-CVD), magnetron sputtering, and plasma-assisted diamond growth. Understanding their individual and combined effects provides a rational basis for optimizing thin-film fabrication processes. Chamber pressure is one of the most influential parameters in thin-film deposition, as it directly affects plasma density, mean free path of reactive species, and surface reaction mechanisms. In PECVD processes, adjusting the chamber pressure enables fine control over the refractive index and thickness of silicon dioxide films, which is particularly important for optoelectronic applications. Studies on ICPECVD have shown that deposition rates of silicon oxide (SiOx) films are more sensitive to pressure variations than to changes in RF power or substrate temperature, highlighting pressure as the dominant growth-controlling factor. Similarly, in magnetoactive plasma-assisted diamond growth, an optimal pressure of approximately 3 Torr was found to promote favorable growth rates and improved crystallinity of diamond films.[18] Input power is another critical parameter that governs plasma energy, ion density, and reactive species generation. In ICPECVD systems, RF power has been identified as the second most influential factor affecting the deposition rate of SiOx films, following chamber pressure. In ECR-CVD, increasing microwave power significantly enhances plasma uniformity and deposition consistency, which is particularly advantageous for large-area coatings required in photovoltaic solar cell manufacturing.[19] Appropriate power optimization is therefore essential to balance deposition rate, uniformity, and film integrity. Substrate temperature plays a decisive role in determining film growth dynamics, stress development, and microstructural evolution. In PECVD-grown SiO_2 films, substrate temperature directly influences growth rate and residual stress, making temperature optimization crucial for high-quality microelectronics applications. In magnetron sputtering processes, elevated substrate temperatures promote surface diffusion of adatoms, leading to denser and more compact film structures during the early stages of growth. For plasma-assisted diamond deposition, a substrate temperature of around 650 °C has been reported as optimal for achieving high crystallinity and improved film quality.[20]

Comparison with Other Deposition Techniques (PVD, Thermal CVD, ALD)

Atomic Layer Deposition (ALD), Physical Vapor Deposition (PVD), and Chemical Vapor Deposition (CVD) are widely used thin-film deposition techniques, each offering distinct capabilities suited to different technological requirements. Among these, ALD has gained particular attention for its ability to deposit ultra-thin, highly conformal films with atomic-scale control over thickness and composition. This level of precision makes ALD especially suitable for complex, high aspect-ratio structures and advanced micro- and nanoelectronic applications. In contrast, PVD and CVD represent more established deposition approaches, each characterized by specific advantages and inherent limitations that influence their applicability across industrial processes. ALD is distinguished by its self-limiting surface reactions, which enable exceptional control over film growth and uniformity. This mechanism allows ALD to achieve excellent conformality on complex three-dimensional architectures, such as semiconductor interconnects and nanoscale features, where uniform coverage is critical. Additionally, ALD typically operates at relatively low temperatures, expanding its compatibility with temperature-sensitive substrates and large-area coatings. However, the sequential nature of ALD results in comparatively slow deposition rates, which can limit throughput for large-scale manufacturing. Ongoing developments, including optimized thermal ALD processes, are addressing these challenges by improving efficiency and scalability.[21] PVD encompasses a range of deposition methods, such as thermal evaporation and ion plating, which rely on the physical transfer of material from a source to the substrate. These techniques are particularly effective for producing metallic and metalized coatings and are widely adopted in industrial applications due to their simplicity and relatively high deposition rates. Nevertheless, the line-of-sight nature of PVD processes often leads to non-uniform film coverage on substrates with high aspect ratios or complex geometries, limiting their effectiveness for ultra-thin or conformal coatings compared to ALD.[22] CVD, in contrast, involves chemical reactions of gaseous precursors at the substrate surface to form solid films, enabling the deposition of dense and high-purity materials. While CVD offers higher deposition rates than ALD and improved step coverage compared to PVD, achieving uniform ultra-thin films on high aspect-ratio structures remains challenging. Furthermore, conventional CVD processes typically require elevated temperatures, which can restrict their use with thermally sensitive substrates. Despite these limitations, CVD provides a balance between film quality and throughput, making it suitable for a broad range of applications in microelectronics, coatings, and materials engineering.[23]

Mechanisms of Film Growth in PECVD

Key Models: Rapid Step-Growth Polymerization (RSGP) and Competitive Ablation Polymerization (CAP)

Rapid Step-Growth Polymerization (RSGP) and Competitive Ablation Polymerization (CAP) are two fundamental models that describe polymer film growth mechanisms in PECVD. These models provide complementary frameworks for understanding how polymeric coatings form under plasma conditions, where energetic species simultaneously drive chemical synthesis and material removal. While RSGP emphasizes orderly polymer formation through stepwise reactions, CAP accounts for the dynamic competition between deposition and ablation processes governed by plasma energy and chemistry. RSGP is based on the stepwise reaction of bifunctional or multifunctional monomers, leading to the gradual formation of polymer chains and cross-linked networks. In this model, polymer growth occurs through successive addition of monomer units, resulting in films with relatively well-defined chemical structures and controlled properties. Because of this predictable growth mechanism, RSGP is particularly suitable for producing thin polymeric films where control over mechanical strength, chemical functionality, and surface characteristics is critical. Such films are widely explored in biomedical coatings and surface modification strategies aimed at improving adhesion, stability, and biocompatibility. A key advantage of RSGP lies in its ability to tailor polymer architecture by adjusting precursor chemistry and deposition conditions, enabling fine control over film performance.[24]

In contrast, the CAP model describes film growth as a balance between polymerization and plasma-induced ablation. Under energetic plasma conditions, incoming species contribute to film formation while simultaneously removing weakly bound or unstable material from the surface. This dynamic equilibrium is strongly influenced by plasma power, ion energy, and the elemental composition of the precursor molecules. CAP explicitly considers plasma sensitivity, where elements with higher electronegativity are more susceptible to fragmentation, thereby altering deposition efficiency and film chemistry. This mechanism is particularly relevant in high-energy PECVD processes, where fragmentation and re-deposition play a dominant role in determining film composition and density. CAP-based growth is advantageous for applications that require robust, chemically stable, or protective coatings, as the continuous ablation process can eliminate loosely bonded structures and promote denser films. Such characteristics are beneficial in surface treatments and protective layers where durability and resistance to environmental stress are essential.[25] By carefully tuning plasma parameters, the interplay between ablation and polymerization can be exploited to achieve specific surface and bulk film properties.

Plasma Polymerization from Organic Precursors

Plasma polymerization is a versatile thin-film deposition technique in which organic precursors are converted into polymeric coatings within a plasma environment. Unlike conventional polymerization, this process involves highly energetic species such as electrons, ions, and radicals, enabling the formation of cross-linked polymer networks with tailored chemical and physical properties. Owing to its ability to precisely modify surface characteristics without affecting bulk material properties, plasma polymerization is widely applied in electronics, biomedical engineering, and surface functionalization technologies. Plasma polymerization can be carried out under either low-pressure or atmospheric-pressure conditions, each offering distinct advantages. Low-pressure plasma polymerization provides enhanced control over film thickness, chemistry, and uniformity, making it particularly suitable for precise surface modifications. In contrast, atmospheric-pressure techniques, including dielectric barrier discharge plasma jets, enable large-area and inline processing and are increasingly employed in applications such as antifouling coatings and tissue engineering.[26] The adaptability of these approaches allows plasma polymerization to be integrated into diverse manufacturing environments. A wide range of organic precursors can be employed in plasma polymerization, extending from synthetic monomers to biogenic compounds. The use of natural oils, terpenes, and other renewable precursors has gained attention due to their compatibility with green chemistry principles and their inherent antimicrobial, biodegradable, and biocompatible properties. Such biogenic plasma polymers are particularly attractive for biomedical and environmentally sustainable applications.[27]

Functionally, plasma-polymerized coatings are extensively used to engineer surface–biomolecule interactions. Nanocoatings produced by plasma polymerization can be designed to promote favorable cell adhesion, regulate protein adsorption, and prevent biofouling, which are critical parameters in biomedical devices and implants.[27] In the electronics sector, plasma-enhanced copolymerization is employed to fabricate low-dielectric-constant films that reduce capacitive delays and power consumption. For example, plasma polymerization of tricyclodecane-based precursors has enabled the formation of mechanically stable films with dielectric constants below 2.5, meeting the stringent requirements of advanced microelectronic devices.[27] The mechanisms underlying plasma polymerization are inherently complex, involving a combination of radical-driven growth, ion bombardment, and surface reactions. Hydrogen plays a critical role in regulating plasma chemistry by influencing the activation, recombination, and termination of reactive species, thereby affecting both deposition rates and film composition. Control over these competing processes remains a key challenge, as variations in plasma parameters can significantly alter film structure and functionality.[28] Continued advances in plasma diagnostics and process optimization are therefore essential to fully exploit the potential of plasma polymerization for advanced functional coatings.

Role of Reactive Species and Ion–Surface Interactions

The growth of thin films in PECVD is governed by the complex interplay between reactive plasma species and ion–surface interactions. Within the plasma, energetic electrons initiate gas-phase reactions that generate a variety of radicals and ions, which subsequently interact with the substrate surface to drive film nucleation and growth. Understanding these interactions is essential for controlling film composition, microstructure, and functional properties, as well as for optimizing deposition conditions across a wide range of PECVD applications. Reactive species play a central role in PECVD film formation. Radicals such as CH, SiH, and CN are commonly produced through plasma-induced fragmentation of precursor gases and exhibit high chemical reactivity at the substrate surface, making them key contributors to film growth. Gas-phase reactions within the plasma generate reactive precursors that directly participate in surface adsorption and incorporation processes, as exemplified by the deposition of hydrogenated amorphous silicon (a-Si:H), where plasma-generated silicon hydrides are critical growth species. The intrinsic reactivity of these radicals is strongly influenced by their electronic structure; species with a doublet electron configuration typically exhibit higher surface sticking probabilities, enhancing their contribution to film deposition.[29] In addition to neutral radicals, ion–surface interactions significantly influence PECVD film growth. Ion bombardment modifies surface chemistry by enhancing surface mobility, promoting densification, and altering film morphology during growth. Energetic ions generated in the plasma can supply localized energy to the growing film, overcoming kinetic barriers that would otherwise require elevated substrate temperatures. This mechanism enables the deposition of high-quality films on temperature-sensitive substrates while maintaining desirable structural properties. Furthermore, ion impacts can induce secondary reactions at the surface, generating new reactive sites and species that further contribute to film growth and structural evolution. The combined effects of reactive species and ion bombardment define the overall film growth mechanism in PECVD. Predictive modeling of these interactions has proven valuable for understanding deposition profiles and growth dynamics, as demonstrated in studies of argon–acetylene magnetron-assisted plasmas, where the balance between radical flux and ion energy determines film thickness and uniformity.[30] Beyond deposition, surface and in-film reactions occurring during growth and post-growth treatments, such as annealing, play a critical role in refining film structure and properties. These processes are particularly important for achieving high-quality, defect-controlled films suitable for advanced electronic and optoelectronic applications.[31]

Control of Crosslinking, Density, and Chemical Functionality

Control over crosslinking, density, and chemical functionality is central to tailoring thin films deposited by PECVD for specific applications. These film characteristics are governed by a combination of process parameters, including precursor chemistry and flow rates, plasma power, reactor configuration, and energy flux at the substrate surface. The interplay of these factors determines the structural integrity, stability, and functional performance of PECVD-grown coatings across biomedical, electronic, and protective applications. Crosslinking within PECVD films can be effectively regulated by modifying the concentration and flow rate of multifunctional precursors or crosslinking agents. For example, increasing the flow of ethylene glycol diacrylate during deposition enhances crosslink density in poly-2-hydroxyethyl methacrylate films, leading to reduced swelling and slower degradation in aqueous environments. Plasma conditions further influence crosslink formation, as higher plasma power increases the fragmentation and activation of precursor species, promoting crosslinking reactions. However, excessive energy input can also generate heterogeneous nanoscale structures, including regions of reduced crosslink density near film interfaces, particularly when feed position and plasma distribution are not optimally controlled.[32] Film density is closely linked to the energetic environment during deposition, with ion bombardment playing a dominant role. Energetic ions transfer momentum to the growing film, promoting densification and reducing free volume within the polymer network. This densification process often occurs at the expense of functional group retention, as higher energy conditions favor bond scission and recombination over the preservation of delicate chemical functionalities. In addition to plasma power, reactor geometry significantly affects film density and crosslinking behavior. Symmetric and asymmetric reactor designs alter electric field distributions and ion energy fluxes, thereby influencing the spatial uniformity of densification and crosslink formation within the film.[33] Chemical functionality in PECVD films is determined by the extent of precursor fragmentation in the gas phase and the reactivity of species arriving at the substrate surface. By carefully balancing plasma energy and precursor flow, it is possible to incorporate specific functional groups, including oxygen- and nitrogen-containing moieties, while maintaining sufficient film stability. This balance is particularly critical in applications such as low-k dielectric materials, where plasma-induced crosslinking is required to enhance thermal and mechanical robustness without excessively increasing film density or dielectric constant. Controlled crosslinking under optimized PECVD conditions therefore enables the production of chemically functional yet structurally stable films suitable for advanced semiconductor technologies.[34] Table 2 summarizes the quantitative relationships between PECVD process parameters, coating structure, and drug-release outcomes across included studies. Median values and interquartile ranges are reported for burst release, Korsmeyer–Peppas parameters (k and n), and t_{50}, highlighting consistent trends despite methodological heterogeneity.

Types of Biocompatible PECVD Coatings

Plasma Polymers Derived from Monomers (e.g., HMDSO, TEOS, Acrylics)

Plasma polymers synthesized from monomers such as HMDSO, tetraethylorthosilicate (TEOS), and acrylic compounds are widely produced using PECVD and plasma-induced polymerization techniques. These plasma-based approaches enable the deposition of ultrathin, highly adherent polymeric films under low-temperature conditions, making them suitable for temperature-sensitive substrates. The physicochemical characteristics of the resulting coatings are strongly dependent on both the chemical structure of the monomer and the plasma operating parameters, including power input, duty cycle, and discharge mode. Silicon-containing monomers such as HMDSO and TEOS are particularly attractive for plasma polymerization due to their hybrid organic–inorganic structures, which promote the formation of conformal and hydrophobic coatings on a wide range of substrates.[35] Plasma-polymerized HMDSO films typically exhibit

Table 2 | 10 key studies on PECVD for creating biocompatible coatings that control drug release from medical devices

S. No	Substrate	Precursor	Plasma Mode/Parameters	Film Properties	Drug	Release Metrics	Biocompatibility Outcomes	Model Type	Limitations	References
1	Si wafers, stents	Hexamethyldisiloxane (HMDSO)	RF-PECVD; 13.56 MHz, 50–200 W, 0.1–1 Torr	Thickness: 50–500 nm; WCA: 70°; Crosslinked siloxane	N/A (bioactive surface)	N/A	EC attachment ↑ 3×; SMC proliferation ↓	*In vitro* (EC/SMC)	No drug release data; short-term assays	101
2	Polymers/implants	Acrylic acid	PECVD; 100 W, Ar carrier, RT	Thickness: 20–100 nm; COOH density: 10^16/cm2	Antibiotics (model)	Zero-order over 30 days	Cytocompatible (MTT >90%)	*In vitro* release	Limited substrate types; model drugs	102
3	Mg alloy stents	PLGA + rapamycin	RF-PECVD; 300 W, O_2 plasma, 0.5 Torr	Thickness: 2 μm; Roughness: 50 nm	Rapamycin	70% release in 28 days (HPLC)	No restenosis; corrosion rate ↓ 80%	*In vivo* (rabbit iliac)	Small n = 6; short 1-month follow-up	103
4	Ti implants	C_2H_2, NH_3	DC-PECVD; 500 V, 10 Pa, 5 minutes	Amorphous C:N; Thickness: 100 nm	Silver ions	Burst 20% day 1, 90% by day 7	Antimicrobial (biofilm ↓99%); Cytocompatible	*In vitro* (S. aureus, fibroblasts)	No long-term release; Ag cytotoxicity risk	104
5	Catheters	Organosilanes	iPPECVD; Pulsed RF, 100 W, He carrier	Ultrathin 10 nm; Bioinert (WCA 90°)	Heparin	Sustained 50% over 14 days	Hemocompatible (clotting time ↑ 2×)	*In vitro* (platelet agg.)	Preclinical only; heparin instability	105
6	Collagen films	TetraEGDMA	Catalyst-free PECVD; 50 W, Ar/O_2, RT	PEG-like; Thickness: 50 nm; Cell repellent	Model hydrophilic drug	Diffusion-controlled (Fickian)	Fibroblast repulsion (>95%)	*In vitro* co-culture	Collagen-specific; mechanical stability?	106
7	SS stents	PEVA + curcumin	Ar/O_2/N plasma; 0–45 seconds exposure	Crosslinked; Thickness: 5 μm	Curcumin	↓ Burst to 5–50 μg/14 days	Anti-inflammatory (IL-6 ↓)	*In vitro/in vivo* (rat)	Variable plasma times; curcumin photostability	107
8	Si wafers/stents	PEVA	O_2/Ar/N_2 plasma; RT, variable time	Increased crosslinking	Curcumin	Plateau release <50 μg/14 days	Endothelial coverage ↑	*In vitro* (HUVEC)	No *in vivo*; burst control incomplete	108
9	Implants	Acrylic monomers	RF-PECVD; 200 W, N_2, 0.2 Torr	Tailored hydrophilicity	Antibiotics	Tunable profile (zero-order)	MTT viability 95%; Antibacterial	*In vitro* (S. epidermidis)	Single drug; lab-scale only	109
10	Stents/catheters	Si-precursor + NH_3/O_2	Two-step DC/RF PECVD; 50–700 W	Bioactive N/O functional; 100 nm	Anti-thrombotic agents	Sustained >12 weeks	EC attachment ↑; No thrombosis	*In vitro/in vivo* (porcine)	Patent data; limited peer-review metrics	110

Each entry details critical parameters including substrate materials, plasma precursors and conditions, resulting film characteristics, incorporated therapeutics, quantitative release kinetics, biological performance metrics, testing models, and study limitations. The compilation illustrates process-structure-property relationships across applications like stents, implants, and catheters, highlighting PECVD's versatility in achieving tunable, sustained drug elution with favorable cytocompatibility and antimicrobial outcomes.

superior retention of monomer-derived functional groups, especially when deposited at shorter treatment times and lower duty cycles, resulting in enhanced hydrophobicity and chemical stability. In contrast, plasma polymers derived from TEOS often display compositional variations that are sensitive to the discharge regime. Pulsed plasma conditions have been shown to increase carbon incorporation in pp-TEOS films compared to continuous-wave plasmas, thereby modifying film density and surface chemistry.[36]

Plasma-induced polymerization of acrylic monomers relies on the ionization and excitation of gaseous or vaporized precursors, leading to the formation of highly crosslinked and chemically complex polymer networks. This technique is particularly advantageous for curing liquid coatings on substrates with complex geometries, as the plasma provides a uniform spatial distribution of reactive species and enables precise microstructuring without the need for thermal curing. Such control allows for the fabrication of functional coatings with tailored mechanical and chemical properties.[37] A common characteristic of plasma polymers is the incorporation of oxygen-containing groups, which can influence long-term stability due to the presence of trapped free radicals within the film matrix. Over time, post-deposition reactions with atmospheric oxygen can alter surface chemistry and material properties. Strategies such as introducing controlled amounts of water vapor during polymerization have been shown to reduce free radical concentration and limit oxygen uptake, thereby improving film stability and preserving functional performance. Owing to their conformality, durability, and low-temperature processing, plasma-polymerized HMDSO, TEOS, and acrylic films find extensive applications as protective and functional coatings on textiles, metals, and polymeric substrates.[38]

Diamond-Like Carbon (DLC) and Functionalized Hydrocarbon Films

Diamond-like carbon (DLC) and functionalized hydrocarbon films represent a class of advanced coating materials distinguished by their exceptional mechanical, chemical, and biological performance. DLC films consist of amorphous carbon with a mixed sp^2/sp^3 bonding structure, imparting diamond-like characteristics such as high hardness and chemical inertness. When integrated with polymeric substrates, these films form multifunctional composites that combine the durability of DLC with the flexibility and processability of polymers, thereby expanding their applicability across bioengineering, electronics, optics, and protective technologies. A defining feature of DLC films is their outstanding hardness and wear resistance, which make them highly effective as protective coatings in mechanically demanding environments. In addition to mechanical robustness, DLC exhibits excellent biocompatibility, supporting cell adhesion and proliferation without eliciting adverse inflammatory responses. This property has driven significant interest in biomedical applications, particularly for surface modification of polymer-based medical devices and implants. From a functional standpoint, DLC films also display favorable thermal stability, high electrical resistivity, and low dielectric constants, attributes that are advantageous for electronic and optical components where insulation and thermal endurance are critical. The application scope of DLC coatings is broad and continues to expand. In the biomedical field, DLC-coated polymers offer enhanced surface durability and biocompatibility, improving device longevity and patient safety. In electronics and optics, the low friction coefficient and high wear resistance of DLC are exploited in components such as hard disk drives, optical lenses, and microelectromechanical systems, where surface reliability is paramount. Furthermore, DLC-coated polymer films exhibit superior gas barrier properties, which are particularly valuable in packaging applications and protective layers where resistance to gas permeation is required. Advances in deposition and functionalization techniques have further enhanced the performance of DLC-based systems. Modern plasma-assisted and ion beam deposition methods enable the formation of dense, uniform, and void-free DLC films, offering improved control compared to conventional sputtering approaches. The integration of DLC with polymer substrates allows for the development of cost-effective and flexible composite materials without compromising surface hardness or chemical stability. Despite these advantages, challenges remain, particularly related to interfacial adhesion and fracture behavior arising from mechanical mismatches between rigid DLC layers and compliant polymer substrates. Addressing these issues is essential for optimizing the reliability and long-term performance of DLC–polymer composite systems.[39,40]

Metal–Organic PECVD Coatings for Tailored Surface Properties

Metal–organic PECVD has emerged as a powerful surface-engineering technique for the fabrication of functional thin-film coatings with precisely tunable properties. By confining modifications to the near-surface region, PECVD enables substantial enhancement of material performance without compromising bulk characteristics. The use of plasma activation in combination with metal–organic precursors provides exceptional control over film composition, structure, and thickness, making this approach highly attractive for applications in microelectronics, aerospace, automotive, and biomedical sectors. A key advantage of metal–organic PECVD lies in its ability to tailor surface properties such as wettability, adhesion, and corrosion resistance through controlled variation of plasma parameters and precursor chemistry. By adjusting the degree of fragmentation and incorporation of metal–organic species, coatings with targeted chemical functionalities and microstructures can be achieved, allowing fine control over interfacial interactions and surface reactivity. The incorporation of metal-containing precursors, including chromium-based compounds, has been shown to significantly enhance mechanical strength, wear resistance, and protective performance, particularly under demanding operational conditions.[41]

Beyond single-component systems, the integration of organic and inorganic additives within PECVD coatings offers synergistic improvements in mechanical robustness and electrochemical stability. Such hybrid coatings exhibit enhanced resistance to corrosion and degradation in aggressive environments, broadening their applicability in industrial settings exposed to chemical or mechanical stress. These multifunctional characteristics underscore the versatility of metal–organic PECVD as a platform for advanced surface design. An additional and distinctive feature of certain PECVD coatings is their ability to exhibit regenerative surface behavior. Siloxane-based films, for example, can undergo post-polymerization surface segregation, where short polymer chains migrate to the surface and restore functionality after surface depletion or damage. This self-renewing mechanism contributes to sustained performance over time, particularly in applications requiring long-term surface stability. Owing to these attributes, metal–organic PECVD coatings are widely employed in optics and optoelectronics, as well as in protective coatings for automotive and aerospace components. Their adaptability to application-specific requirements, including corrosion protection for offshore and industrial infrastructures, highlights the continuing potential of PECVD-derived functional coatings. Ongoing developments in precursor chemistry and plasma process control are expected to further expand the performance envelope and industrial relevance of metal–organic PECVD technologies.[42]

Hybrid Multifunctional Films for Biomedical Integration

Hybrid multifunctional films have gained increasing attention in biomedical integration due to their ability to simultaneously incorporate multiple desirable properties within a single coating or thin-film system. By combining organic and inorganic components, these films are engineered to deliver biocompatibility, antibacterial activity, optical functionality, and mechanical stability, thereby addressing the complex performance requirements of modern biomedical applications. Such multifunctionality makes hybrid films particularly attractive for use in implantable devices, surface coatings, biosensors, and controlled drug delivery platforms. A defining characteristic of hybrid multifunctional films is their capacity to integrate diverse functional properties through rational material design. For example, the incorporation of silver nanoparticles within hybrid matrices imparts strong antibacterial activity, while the addition of silicon quantum dots enables visible-light fluorescence for imaging or diagnostic purposes. When combined with fluorosilane components, these films can also exhibit high surface contact angles, resulting in self-cleaning and anti-fouling behavior that is advantageous for long-term biomedical use.[43] The coexistence of such functionalities within a single film highlights the versatility of hybrid architectures.

Biocompatibility and bioactivity are central to the successful biomedical deployment of hybrid films. Silicon-based hybrid nanolayers have demonstrated excellent cytocompatibility, supporting enhanced cell adhesion and proliferation compared with conventional substrates such as glass. This makes them particularly suitable for coating complex or irregular biomedical surfaces without compromising biological performance. Similarly, multifunctional bioactive nanostructured films have been engineered to improve mechanical strength and tribological performance while preserving bioactivity, a critical balance for load-bearing or dynamic biomedical environments. The synthesis and structural design of hybrid multifunctional films play a pivotal role in defining their performance. Advanced fabrication strategies, including molecular layer deposition and self-propagating high-temperature synthesis, enable precise control over film thickness, composition, and functional distribution at the nanoscale. In addition, hybrid composites such as metal–organic frameworks offer high surface areas and tunable pore architectures, which are particularly beneficial for applications requiring controlled drug loading and release. Collectively, these advances underscore the potential of hybrid multifunctional films as next-generation materials for integrated biomedical solutions.[44,45]

Physicochemical Properties and Characterization

The physicochemical properties and characterization of materials, particularly in the context of nanostructuring and surface functionalization, are critical for enhancing their functional performance across diverse applications. Key properties include morphology, thickness, surface energy, chemical composition, bonding, wettability, adhesion, and mechanical behavior. Plasma-driven techniques have emerged as versatile tools for tailoring these characteristics, enabling the development of materials with optimized functionalities suited for biosensing, catalysis, biomedical coatings, and other advanced applications. Morphology, thickness, and surface energy are fundamental determinants of material performance. Surface features such as grain size and roughness, as revealed by AFM analyses, significantly influence both surface energy and mechanical properties. Variations in plasma processing parameters, such as duty cycles, can modulate these morphological characteristics, thereby impacting interactions with biological molecules and overall material stability.[46] Surface energy, in particular, plays a pivotal role in applications where molecular adsorption and interfacial interactions are critical, such as in biosensors and biointerfaces. Chemical composition and bonding are essential for defining reactivity and functional capabilities. Spectroscopic techniques including FTIR, XPS, and Raman spectroscopy provide detailed insights into bonding states and the presence of functional groups, such as amines in plasma-polymerized films, which are crucial for subsequent surface modifications and biofunctionalization.[47] These chemical characteristics directly influence material interactions, determining their suitability for catalysis, sensing, and other surface-sensitive applications. Wettability, adhesion, and mechanical properties are highly responsive to surface modification strategies. Plasma treatments can be precisely applied to adjust hydrophilicity, surface tension, and adhesive strength, thereby enhancing biocompatibility and interfacial bonding with substrates. Mechanical properties, including scratch resistance and critical force thresholds, are also modulated through plasma processing, with process parameters such as duty cycle influencing the robustness and stability of the resulting films.[46] Plasma-driven nanostructuring and surface functionalization provide a powerful approach for engineering surfaces at the micro- and nanoscale. These techniques enable the controlled incorporation of functional chemical groups and the modification of surface topography, resulting in improved hydrophilicity, mechanical integrity, and overall performance. Despite these advantages, the underlying mechanisms governing interactions between plasma species and material surfaces remain incompletely understood, highlighting the need for further research to optimize plasma-based modifications for targeted applications.[48] Collectively, the integration of plasma-assisted techniques with comprehensive material characterization offers a robust pathway for designing advanced materials with tailored physicochemical properties. Continued investigation into plasma–material interactions will further enhance the precision and applicability of nanostructured and functionalized surfaces across multiple technological domains (Figure 3).

Biocompatibility and Biofunctionality

In Vitro Biocompatibility (Cell Adhesion, Viability, and Proliferation Tests)

In vitro biocompatibility assessments, including evaluations of cell adhesion, viability, and proliferation, are fundamental for determining the suitability of PECVD coatings in biomedical applications. These tests provide critical insights into how effectively cells interact with coated surfaces, which directly impacts the integration and performance of implants within biological systems. Surface properties, such as roughness, porosity, and chemical composition, play pivotal roles in mediating these cellular responses, as highlighted by recent studies. Cell adhesion is strongly influenced by both the chemical and topographical characteristics of coatings. Nitrogen-doped DLC films deposited on Ti6Al4V alloy via PECVD have been shown to significantly enhance cell adhesion, attributable to the presence of nitrogen functional groups that improve surface bioactivity.[49] Similarly, increased surface roughness and porosity provide additional anchoring points and larger surface areas for cellular attachment, further promoting adhesion.[50] These findings underscore the importance of engineering surface features to optimize initial cellular interactions. Cell viability is another critical metric for assessing biocompatibility. Niobium coatings produced by magnetron sputtering exhibited no cytotoxic effects, indicating their bioinert nature and ability to support cellular survival. Electronic properties of coatings, such as the band gap and conductivity of amorphous silicon carbide (a-SiC:H) films, can indirectly support cell viability by enhancing hemocompatibility and reducing thrombogenic responses.[51] These results highlight the interplay between surface chemistry, electronic characteristics,

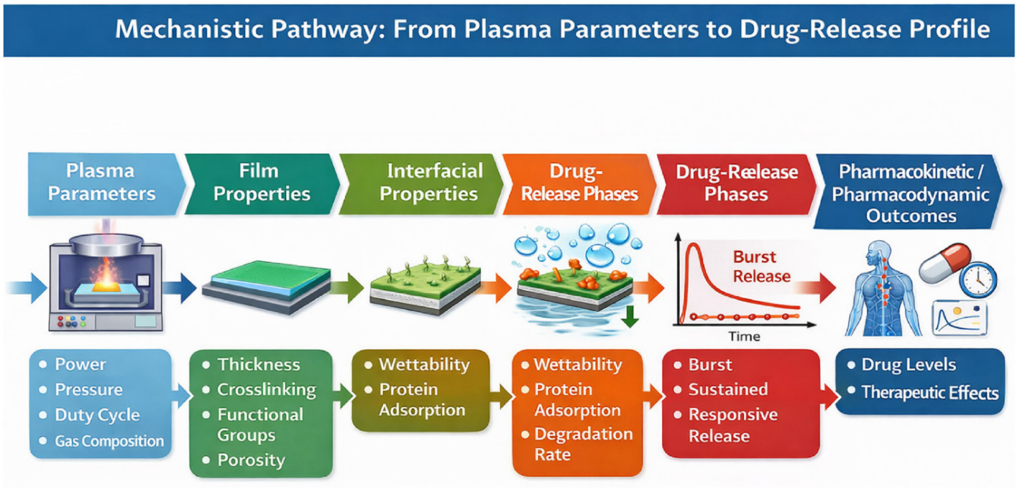

Fig 3 | The diagram depicts the mechanistic pathway linking PECVD plasma parameters to the final drug-release profile and therapeutic outcome. Variations in plasma power, pressure, duty cycle, and gas composition govern key film properties such as thickness, crosslinking density, functional group incorporation, and porosity. These structural and chemical features, in turn, determine interfacial characteristics including wettability, protein adsorption, and degradation behavior at the biomaterial–tissue interface. Collectively, these interfacial properties regulate distinct drug-release phases initial burst, sustained diffusion-controlled release, and stimulus-responsive release thereby shaping pharmacokinetic and pharmacodynamic outcomes. This pathway highlights how precise plasma process control enables rational design of coatings with predictable and tunable drug-delivery performance and cellular health. Cell proliferation on PECVD coatings is closely linked to surface energy, chemical functionality, and treatment methods. Nitrogen-doped DLC films have been reported to significantly promote the proliferation of 3T3-E1 osteoblast cells, suggesting potential utility in bone regeneration and orthopedic applications.[52] Tantalum pentoxide coatings subjected to argon ion treatment demonstrated enhanced proliferative activity of bone marrow cells, illustrating the influence of surface modification on cellular growth dynamics.[53] Such findings emphasize that controlled surface engineering can effectively modulate cell proliferation rates. While these studies demonstrate the beneficial impact of surface modifications on biocompatibility, it is important to recognize that cellular responses are highly dependent on the type of coating, cell lineage, and intended biomedical application. Comprehensive evaluations integrating surface characterization with in vitro cellular assays are therefore essential to optimize PECVD coatings for clinical use. By tailoring surface chemistry, topography, and treatment parameters, PECVD coatings can be designed to maximize adhesion, viability, and proliferation, ultimately improving the functional integration of implants within biological environments.

In Vivo Performance of PECVD-Coated Implants

The in vivo performance of PECVD-coated implants is a critical focus in biomedical research, emphasizing the enhancement of biostability, biocompatibility, and functional integration within biological environments. PECVD coatings, including SiOx, silicon nitride, and amorphous silicon carbide (a-SiC), have been extensively studied for their dissolution behavior, compatibility with host tissue, and potential to promote osteogenesis. These coatings are typically applied to substrates such as silicon chips and titanium to improve implant longevity and performance in vivo. Biostability and dissolution rates are key parameters influencing implant reliability. PECVD silicon nitride and SiOx films exhibit dissolution rates of approximately 2.0 nm/day and 3.5 nm/day, respectively, when implanted subcutaneously in rat models. These rates are considerably higher than those observed for LPCVD silicon nitride, which dissolves at 0.33 nm/day, indicating that PECVD films possess relatively lower long-term stability.[54] In contrast, PECVD-deposited a-SiC demonstrates exceptional stability, showing no measurable dissolution at physiological temperatures and thus outperforming LPCVD silicon nitride in terms of biostability.[54]

Biocompatibility and osteogenic potential are also enhanced by PECVD surface modifications. Titanium surfaces functionalized with amino groups via PECVD promote osteogenesis, as evidenced by increased new bone formation in miniature pig models compared to unmodified titanium.[55] Similarly, PECVD a-SiC coatings on microelectrodes implanted in rabbit cortical tissue elicited no chronic inflammatory responses, demonstrating excellent biocompatibility and maintaining neuronal viability in vivo.[56] These findings underscore the capacity of PECVD coatings to support cellular integration and tissue compatibility. Comparative studies with alternative coatings provide additional context for evaluating PECVD performance. Zirconium-based coatings, although not deposited via PECVD, displayed similar biocompatibility in rat models without inducing adverse biological effects. Similarly, implants coated with bioactive glass or plant extracts exhibited favorable tissue responses, offering benchmarks for assessing PECVD modifications.[57] Overall, PECVD coatings demonstrate considerable promise in enhancing implant functionality through improved biocompatibility and osteogenic potential. However, the relatively higher dissolution rates of some PECVD films highlight the need for further optimization to achieve long-term stability. Future research should focus on balancing functional enhancement with durability, tailoring PECVD processes to maximize both the biological performance and lifespan of coated implants across diverse medical applications.

Antibacterial and Antifouling Surface Modifications

Antibacterial and antifouling surface modification using PECVD has emerged as an effective strategy to mitigate bacterial adhesion and biofilm formation on biomedical devices. By enabling precise control over surface chemistry, morphology, and energy without altering bulk material properties, PECVD facilitates the development of functional coatings that address infection-related complications while maintaining mechanical and structural integrity. This versatility makes PECVD particularly attractive for implantable and long-term medical applications. Antibacterial functionality can be achieved through plasma-assisted deposition of chemically active polymeric and carbon-based films. Initiated chemical vapor deposition (iCVD) has been employed to fabricate graded polymer coatings containing poly (dimethyl amino methyl styrene) (DMAMS) and vinyl pyrrolidone (VP), which exhibit strong bactericidal activity. These coatings demonstrate greater than 99.9% efficacy against both Gram-negative and Gram-positive bacteria, such as *Escherichia coli* and *Bacillus subtilis,* largely due to the high surface zeta potential associated with DMAMS-rich regions.[58] Similarly, fluorinated diamond-like carbon (F-DLC) films deposited by PECVD show enhanced antibacterial performance, where increasing fluorine content reduces bacterial adhesion by lowering surface free energy and modifying surface roughness, consistent with thermodynamic adhesion models.[59]

Antifouling behavior is primarily governed by surface chemistry and topography, both of which can be finely tuned through plasma-based techniques. Plasma-assisted modification enables the creation of surfaces that resist nonspecific protein adsorption and bacterial attachment, thereby limiting early-stage biofilm development without compromising substrate integrity.[60] Incorporation of hydrophilic components such as VP into polymer coatings further enhances antifouling performance while improving biocompatibility. Notably, such coatings retain their resistance to bacterial adhesion even after repeated microbial exposure and rigorous washing cycles, indicating robust durability under physiologically relevant conditions.[61] Despite these advantages, challenges remain in ensuring the long-term stability and sustained antibacterial efficacy of PECVD-modified surfaces in complex biological environments. Future strategies may involve integrating natural antimicrobial agents or bio-inspired functionalities into PECVD coatings to further enhance performance while avoiding the use of conventional antibiotics. Such developments could provide durable, synthetic, and antibiotic-free solutions for infection-resistant biomedical devices.

Blood, Protein, and Tissue Compatibility

PECVD has emerged as an effective surface-engineering strategy to improve blood, protein, and tissue compatibility of biomaterials used in medical devices. By enabling the formation of thin, conformal, and chemically tailored coatings, PECVD can modulate surface–biological interactions without altering the bulk properties of the underlying substrate. This capability is particularly valuable for implants and blood-contacting devices, where surface chemistry plays a decisive role in determining biocompatibility and long-term performance. Enhancement of blood compatibility through PECVD coatings has been demonstrated in several studies. Amorphous hydrogenated silicon carbide (a-SiC:H) coatings deposited by PECVD significantly improve the thrombus resistance of cardiovascular implants by modifying electrochemical interactions between the material surface and blood components, thereby reducing platelet activation and thrombus formation.[62] Similarly, PECVD-treated dental implant surfaces have shown clotting times comparable to uncoated controls, indicating that such coatings do not adversely affect coagulation and are compatible with blood contact.[63]

Protein compatibility is another critical factor governing the biological response to implanted materials, as the initial layer of adsorbed proteins mediates subsequent cellular and hematological interactions. PECVD-derived zwitterionic coatings have proven highly effective in resisting nonspecific protein adsorption, thereby preserving surface functionality and reducing the risk of thrombosis and inflammatory responses.[11] The composition and conformation of adsorbed proteins are closely linked to blood compatibility, underscoring the importance of surface engineering strategies that control protein–surface interactions.[64] Tissue compatibility of PECVD-modified materials has also been reported, particularly in the context of fibrous scaffolds for regenerative applications. Although plasma-enhanced chemical (PEC) fibrous scaffolds may exhibit initial thrombogenicity, the incorporation of anticoagulant agents such as heparin markedly improves blood compatibility while maintaining favorable tissue responses. In vivo evaluations further revealed no acute inflammatory reactions and effective cell infiltration, highlighting the suitability of PECVD-engineered scaffolds for tissue engineering and implant integration.[65] Overall, PECVD offers a versatile and powerful platform for enhancing blood, protein, and tissue compatibility of biomaterials. However, the biological performance of PECVD coatings is highly dependent on coating composition, thickness, and deposition parameters, as well as the intended clinical application. Continued optimization and application-specific design are therefore essential to fully exploit the potential of PECVD in advanced biomedical devices.

Applications in Controlled Drug Release Systems

PECVD as a Platform for Stimuli-Responsive (pH, Temperature, Light) Drug Release

PECVD has gained increasing attention as a flexible surface-engineering approach for the development of stimuli-responsive drug delivery systems. By enabling the deposition of ultrathin, conformal, and chemically tunable coatings, PECVD allows drug release to be regulated in response to specific internal or external stimuli. Such responsiveness is particularly advantageous for site-specific therapies, including cancer treatment, where the tumor microenvironment (TME) presents distinct physicochemical cues that can be exploited to achieve controlled and localized drug delivery. pH-responsive drug release systems fabricated using PECVD are especially relevant for targeting tumors, as the TME typically exhibits a more acidic pH than healthy tissues. This difference can be harnessed to trigger selective drug release at the tumor site, thereby reducing off-target exposure and systemic toxicity.[66] PECVD enables the synthesis and surface functionalization of polymers and nanoparticles whose physicochemical properties, such as solubility or permeability, change in response to pH variations, allowing precise modulation of release kinetics and improved therapeutic efficiency.[67] Temperature-responsive drug delivery systems represent another important application of PECVD-engineered coatings. Slightly elevated temperatures associated with inflamed or malignant tissues can act as triggers for drug release, enhancing selectivity toward diseased sites.[68] Through PECVD, temperature-sensitive coatings can be designed to undergo reversible structural or phase transitions at predefined thermal thresholds, thereby enabling controlled and predictable drug liberation in response to localized hyperthermia or pathological temperature changes.[69] Light-responsive drug release platforms offer the additional advantage of external and spatiotemporal control over therapeutic delivery. By incorporating photo-responsive functional groups into PECVD-deposited films, drug release can be activated on demand using specific light wavelengths, allowing precise targeting and timing of therapy.[70] PECVD facilitates the stable integration of such photo-active moieties into delivery systems, supporting light-triggered release mechanisms with high spatial resolution. Despite the significant potential of PECVD-based stimuli-responsive drug delivery systems, several challenges remain. Ensuring long-term biocompatibility, preventing premature drug leakage, and maintaining stable responsiveness under physiological conditions are critical considerations. Moreover, the integration of multiple stimuli-responsive mechanisms within a single platform could further enhance targeting specificity and therapeutic efficacy, although such multifunctional systems require careful material design and optimization.

Surface Functionalization for Drug Adsorption or Encapsulation

PECVD has emerged as a powerful and versatile technique for surface functionalization in drug adsorption and encapsulation applications. By enabling precise control over surface chemistry, thickness, and morphology of deposited films, PECVD facilitates the fabrication of biocompatible and functionally tailored interfaces without altering the bulk properties of the underlying substrates. These attributes make PECVD particularly attractive for advanced drug delivery systems, where surface characteristics critically govern drug loading, stability, and release behavior. One of the key strengths of PECVD lies in its ability to introduce specific chemical functionalities onto surfaces with high precision. For example, amine-functionalized polyethylene glycol (aPEG) thin films fabricated via PECVD exhibit excellent biocompatibility and low nonspecific adsorption, while providing reactive sites for the immobilization of biomolecules. Such functionalized surfaces are highly relevant for biomedical applications, including biosensing, disease diagnostics, and implantable devices, where controlled biological interactions are essential.[71] More broadly, PECVD allows fine tuning of both chemical composition and physical properties of thin films, enabling the rational design of interfaces optimized for drug encapsulation and sustained release.[72] PECVD and related vapor-phase deposition techniques have also been successfully applied to the encapsulation of active pharmaceutical ingredients. These approaches allow drugs to be coated with nanostructured films that regulate diffusion and degradation, thereby achieving controlled and prolonged drug release. Such vapor-deposited coatings support the development of next-generation drug delivery devices by offering uniform coverage, solvent-free processing, and compatibility with temperature-sensitive compounds.[73] In this context, iCVD has demonstrated particular utility in coating drug particles to impart enteric release properties, further highlighting the potential of vapor-phase techniques for precise control over drug release profiles.[74]

Although PECVD offers significant advantages in terms of versatility and process control, alternative surface functionalization strategies provide complementary capabilities. Techniques such as iCVD enable the fabrication of superhydrophobic and highly reactive coatings suitable for post-functionalization, while non-covalent approaches using host–guest systems like cucurbit[7]uril (CB[7]) offer modular and reversible platforms for drug delivery. Simpler chemical modification methods, including organosilane functionalization of inorganic supports, emphasize efficiency and scalability for applications such as adsorption and catalysis.[75] Collectively, these approaches underscore the diverse toolkit available for surface engineering, with PECVD occupying a central role in the design of advanced, functionalized drug delivery interfaces.

PECVD Smart Polymer Coatings Enabling Tunable Permeability

PECVD derived smart polymer coatings have emerged as an effective strategy for achieving tunable permeability, a property that is central to applications such as chemical sensing, membrane separations, and controlled drug release. The strength of PECVD lies in its capacity to precisely tailor film characteristics through controlled deposition conditions, enabling the fabrication of coatings that function either as effective diffusion barriers or as selectively permeable membranes. This tunability is governed by a detailed understanding of film growth mechanisms, pore size distribution, and surface chemistry, all of which collectively dictate the transport behavior of small molecules across the deposited films. The structural features of PECVD films play a decisive role in regulating permeability. Control over film thickness and chemical composition allows permeability to be finely adjusted according to application requirements. By varying precursor chemistry and plasma process parameters, PECVD can generate dense, crosslinked coatings that restrict molecular transport, as well as more open, polymer-like networks that permit selective diffusion. In this context, the distribution of nanoscale pores and the nature of surface functional groups critically influence solubility–diffusion processes and molecular selectivity, making structure–property relationships central to permeability control. The versatility of PECVD coatings has led to their widespread adoption across diverse technological domains. In electronics, such films are routinely employed as dielectric or semiconducting layers, where controlled permeability and barrier properties are essential for device stability and performance. Beyond conventional applications, PECVD enables the fabrication of smart coatings whose permeability can respond dynamically to environmental stimuli such as light, pH, or temperature. The ability to modify film properties sequentially without breaking vacuum further enhances process flexibility, while the inherent conformality of PECVD coatings allows uniform coverage of complex and high–surface-area substrates, expanding their applicability in permeation-driven systems. Despite these advantages, challenges remain in achieving molecular-level precision over film architecture to ensure reproducible and predictable permeability. Variations in plasma chemistry, energy input, and precursor fragmentation can introduce heterogeneity that complicates structure–transport correlations. Consequently, ongoing research is focused on refining deposition strategies, improving in situ diagnostics, and exploring new polymer chemistries to better link nanoscale film structure with macroscopic transport behavior. While alternative deposition techniques may offer simplicity or cost benefits, they generally lack the same degree of control over film composition and permeability, underscoring the unique value of PECVD for the development of highly specialized, tunable smart coatings.[76,77]

Integration in Nanocarriers, Microneedles, and Biodegradable Devices

The integration of PECVD into the design of nanocarriers, microneedles (MNs), and biodegradable medical devices has attracted growing attention as an advanced strategy to improve drug delivery efficiency and therapeutic performance. PECVD enables precise control over surface chemistry, coating thickness, and material architecture, which are critical determinants of device functionality, biocompatibility, and patient compliance. These attributes are particularly relevant for minimally invasive and biodegradable systems, where subtle changes in material properties can strongly influence mechanical behavior, degradation kinetics, and drug release profiles. In the context of MN technology, PECVD has emerged as a valuable tool for surface modification and performance optimization. MNs are widely explored for transdermal drug delivery because they painlessly bypass the stratum corneum while enabling localized or systemic drug administration. PECVD-deposited thin films on MN surfaces can enhance mechanical robustness, reduce fracture risk during skin insertion, and modulate drug diffusion pathways, thereby improving delivery efficiency and reliability.[78] Furthermore, when biodegradable polymers are employed such as in insulin-delivering MN systems—PECVD coatings offer a means to achieve uniform surface modification, allowing finer control over polymer degradation rates and sustained drug release behavior.[79] PECVD also plays an important role in the development of nanocarrier-based drug delivery platforms, either as standalone systems or in combination with MNs. Surface modification of nanocarriers via PECVD can improve their physicochemical stability, drug-loading capacity, and interactions with biological interfaces, ultimately enhancing therapeutic efficacy. In more advanced applications, PECVD enables the incorporation of functional coatings or active moieties, such as photosensitizers, facilitating multifunctional nanocarriers for combined drug delivery and photothermal or photodynamic therapies.[80]

For biodegradable medical devices, PECVD provides additional advantages by enabling the deposition of thin, biocompatible coatings that regulate degradation kinetics while preserving or enhancing mechanical integrity. Such control is essential for applications requiring predictable device lifespan and controlled release of encapsulated therapeutics. Notably, fabrication approaches such as electro-drawing of biodegradable polymer MNs can be further enhanced by PECVD surface treatments, allowing the creation of complex, mold-free device architectures with tailored surface and bulk properties, thereby simplifying manufacturing workflows. Despite its clear advantages, the broader translation of PECVD into medical device manufacturing faces challenges, including scalability, process complexity, and the need for specialized infrastructure. Addressing these limitations through process optimization and cost-effective system design will be essential to fully harness the potential of PECVD in next-generation nanocarriers, MNs, and biodegradable therapeutic devices.[81]

Recent Advances and Emerging Trends

Pulsed and Field-Enhanced PECVD for Precision Doping and Microstructure Control

Pulsed and field-enhanced PECVD techniques represent important advancements in thin-film engineering, enabling precise control over doping levels, microstructure, and functional properties. By dynamically manipulating deposition parameters such as radio-frequency power, duty cycle, and precursor delivery, these approaches allow fine tuning of optical, chemical, and structural characteristics of deposited films. Such precision is essential for applications in electronics, photonics, and surface engineering, where small variations in composition or morphology can significantly influence device performance. Pulsed PECVD operates by periodically switching between deposition and non-deposition phases, offering enhanced control over film growth kinetics and chemical incorporation. This temporal modulation enables the process to bridge conventional PECVD and ALD, achieving near-digital control over film conformality and thickness uniformity.[82] Adjustment of the pulsed radio-frequency duty cycle has been shown to directly influence the microstructure, optical response, and chemical composition of materials such as hydrogenated amorphous silicon nitride (a-SiNx:H) alloys, allowing tailored film properties for specific functional requirements.[83] Field-enhanced PECVD further expands process capabilities by enabling high-quality film deposition at relatively low temperatures and pressures, making it particularly suitable for thermally sensitive substrates. This approach supports the growth of dense dielectric and semiconducting layers with controlled electrical and optical properties, as demonstrated in silicon-based and oxide materials used in electronic and optoelectronic devices. Its flexibility in material selection and compositional tuning has also been validated in complex systems such as SiO_2–TiO_2 composite films, where precise thickness and stoichiometry control are essential for high-performance antireflection coatings.[25] The high level of control offered by pulsed and field-enhanced PECVD has enabled their application in advanced optical and semiconductor architectures. Pulsed PECVD has been successfully employed in the fabrication of Fabry–Pérot filters and superlattice structures, highlighting its reproducibility and versatility in multilayer film design. Moreover, time-controlled precursor proportioning in these systems allows accurate doping without memory effects, resulting in improved dopant uniformity and enhanced electronic performance in semiconductor materials.[84] Despite their clear advantages, pulsed and field-enhanced PECVD techniques require careful optimization of process parameters to balance deposition rate, film quality, and compositional accuracy. The increased system complexity and sensitivity to operating conditions can present challenges for large-scale industrial implementation. Continued research focused on process stabilization, scalability, and real-time control strategies is therefore essential to fully exploit the potential of these advanced PECVD methodologies in next-generation thin-film technologies.[83]

Plasma-Assisted Hybrid Deposition (PECVD + Magnetron Sputtering, PECVD + ALD)

Plasma-assisted hybrid deposition techniques that integrate PECVD with complementary methods such as magnetron sputtering or ALD have emerged as powerful strategies for fabricating nanostructured and multifunctional coatings. By combining distinct plasma-based processes within a single or sequential deposition framework, these hybrid approaches enable enhanced control over film composition, microstructure, and growth kinetics. Such control is particularly valuable for advanced applications that demand high coating quality, precise thickness regulation, and low-temperature processing. The integration of PECVD with magnetron sputtering leverages the strengths of both techniques to achieve atomically controlled thin films with tailored physical and chemical properties. Plasma assistance during reactive magnetron sputtering improves film densification and compositional uniformity while maintaining relatively high deposition rates. This hybrid strategy allows fine tuning of parameters such as film stress, refractive index, and surface roughness, making it especially attractive for optical and photonic applications, including high-performance interference filter coatings where strict material tolerances are required.[85] Combining PECVD with ALD further extends the capabilities of plasma-assisted deposition by merging atomic-scale thickness control with the flexibility and efficiency of plasma processes. In this configuration, ALD contributes exceptional conformality and monolayer-level precision, while PECVD enables faster growth rates and reduced thermal budgets. This synergy has proven effective for synthesizing dense ceramic thin films and complex nanocomposites, including amorphous hydrocarbon-based coatings with tunable compositions that are difficult to achieve using conventional single-method approaches.[86] Overall, plasma-assisted hybrid deposition techniques offer a versatile platform for engineering advanced nanostructured materials with finely tuned properties. However, the increased process complexity necessitates careful optimization of critical parameters such as plasma power, gas chemistry, and substrate temperature to ensure reproducibility and desired film characteristics. Challenges related to system integration and scalability remain, highlighting the need for continued research to adapt these hybrid methodologies for robust and cost-effective industrial implementation across diverse technological fields.

Green and Atmospheric Pressure PECVD Technologies

Atmospheric pressure plasma-enhanced chemical vapor deposition (AP-PECVD) has emerged as an attractive alternative to conventional low-pressure PECVD, primarily due to its compatibility with industrial manufacturing and its reduced environmental footprint. By eliminating the need for vacuum systems, AP-PECVD enables large-area thin-film deposition with lower capital and operational costs while maintaining coating qualities comparable to those obtained under low-pressure conditions. These attributes make AP-PECVD particularly suitable for functional coatings such as scratch-resistant layers, gas and moisture barriers, and antireflective films used in industrial and consumer products.[87] A key strength of AP-PECVD lies in its scalability and adaptability to continuous production environments. The technology supports air-to-air processing and can accommodate wide substrate formats, allowing seamless integration into roll-to-roll or in-line manufacturing systems. Atmospheric-pressure plasma sources, including microwave and DC Arc-Jet-CVD configurations, enable relatively high deposition rates, typically in the range of 5–100 nm s^{-1} under static conditions, thereby supporting high-throughput industrial processing without compromising film quality.[88] AP-PECVD also offers considerable versatility in terms of materials and processing conditions. A wide range of functional coatings, including SiOx, silicon nitride, titania, and aluminum oxide, can be deposited to meet diverse application requirements. Notably, the ability to form high-quality SiOx films at low temperatures (≤120 °C) extends the applicability of AP-PECVD to temperature-sensitive substrates such as polymers and flexible materials, which are increasingly important in modern device fabrication.[89] From an environmental and economic perspective, atmospheric-pressure operation significantly reduces energy consumption by eliminating vacuum generation and associated infrastructure. In addition, AP-PECVD processes can yield smooth, uniform, and low-contamination coatings, contributing to improved durability and functional performance. Despite these advantages, challenges remain in achieving precise control over film uniformity and properties across large surface areas. Ongoing research is therefore focused on refining plasma sources and process control strategies to expand the applicability of AP-PECVD in advanced fields such as photovoltaics, flexible electronics, and large-area coatings.[90]

Plasma-Derived Nanolayer Composites for Multifunctional Biomedical Devices

Plasma-derived nanolayer composites have gained increasing attention as multifunctional surface engineering strategies for biomedical devices, particularly where simultaneous antibacterial performance and biocompatibility are required. These systems are commonly fabricated via plasma polymerization, a technique that enables fine control over film chemistry, thickness, and nanoparticle incorporation. By integrating metallic nanostructures, most notably silver nanoparticles, within plasma-polymer matrices, these coatings address critical clinical challenges such as device-associated infections while preserving compatibility with surrounding tissues. The antibacterial efficacy of plasma-derived nanolayer composites is largely attributed to the controlled incorporation of silver nanoparticles within amorphous carbon- or nitrogen-containing plasma polymers. Ag/a-C:H:N coatings have demonstrated a substantial reduction in bacterial adhesion, with reports indicating up to 95% inhibition of Escherichia coli attachment over a 24-hour period. Importantly, plasma polymer silver nanocomposites allow tunable Ag^+ release, enabling effective antimicrobial activity against both Gram-negative and Gram-positive bacteria while minimizing cytotoxic effects, thereby achieving a balance between antimicrobial potency and biological safety.[91] Beyond antimicrobial performance, cytocompatibility and bioactivity are central to the clinical applicability of these coatings. Plasma-polymer matrices have been shown to support long-term cytocompatibility, even in the presence of embedded silver nanoparticles, making them suitable for prolonged implantation. Moreover, plasma polymerization offers the unique capability to immobilize or bond bioactive molecules onto device surfaces, expanding the functional scope of nanolayer composites toward therapeutic and regenerative applications.[92] Plasma-assisted silver nanocomposite coatings also exhibit strong resistance to biofilm and clot formation, which are major causes of implant failure and device-associated complications. Recent in vitro and in vivo studies, including murine models, have demonstrated that silver-based plasma nanocoatings significantly inhibit biofilm development and thrombus formation while maintaining hemocompatibility and cytocompatibility. These multifunctional properties are particularly valuable for blood-contacting devices such as catheters and vascular implants.[93] Despite their considerable advantages, challenges remain in ensuring the long-term stability of plasma-derived nanolayer composites and achieving consistent performance across diverse biomedical applications. Variability in silver release kinetics and durability under physiological conditions requires further optimization. Nevertheless, the convergence of plasma processing and nanotechnology continues to offer a powerful platform for the development of next-generation biomedical devices with integrated antibacterial, bioactive, and biocompatible functionalities.[94]

Challenges, Limitations, and Knowledge Gaps

PECVD has emerged as a powerful strategy for fabricating biocompatible coatings in controlled drug release systems; however, its broader translation is constrained by challenges related to reproducibility and scalability. These limitations arise from the complex interdependence between plasma process parameters, coating chemistry, and the structural features that govern drug diffusion and release kinetics. Achieving reliable and predictable performance therefore requires stringent control over both material selection and deposition conditions. Reproducibility remains a major concern in PECVD-based drug delivery coatings, as small variations in chemical composition or crosslinking density can substantially alter drug release behavior. Differences in precursor chemistry, particularly in acrylate-based or polymerizable monomers, may lead to batch-to-batch variability in network structure and permeability, ultimately affecting release profiles. In parallel, process-related parameters such as plasma power, precursor flow rate, and substrate temperature strongly influence film thickness, uniformity, and chemical functionality. Inconsistent control of these variables can result in heterogeneous coatings, undermining the predictability of drug release.[95]

Scaling up PECVD processes introduces additional complexities, especially when transitioning from laboratory-scale substrates to larger or more complex geometries. Reactor design plays a critical role in ensuring uniform plasma exposure and precursor distribution across extended surfaces. Customization of reactor configurations is often necessary to preserve coating homogeneity during scale-up. Moreover, maintaining stable plasma conditions and uniform deposition rates over larger areas becomes increasingly challenging, requiring advanced process optimization strategies to avoid gradients in film properties that could compromise drug delivery performance. Beyond reproducibility and scale-up, biocompatibility and precise control over drug release kinetics remain central design requirements. Surface chemistry is a key determinant of biological response, and PECVD enables the tailoring of surface functionalities through judicious precursor selection and plasma conditions. For example, plasma-deposited polyethylene glycol (PEG) films are widely reported to exhibit excellent biocompatibility due to their resistance to nonspecific protein adsorption. At the same time, controlled drug release can be achieved by regulating film crosslinking density and matrix composition. Emerging approaches, such as aerosol-assisted or open-air plasma deposition, further expand the ability to entrap bioactive agents within plasma-polymer matrices and modulate their release behavior.[96]

Plasma coatings fabricated by PECVD are increasingly investigated as advanced biocompatible platforms for controlled drug release systems. Their appeal lies in the ability to form ultrathin, conformal, and chemically tunable films that maintain long-term stability under physiological conditions. Plasma-polymerized coatings can be engineered at the molecular level to regulate permeability and responsiveness to environmental cues, enabling precise modulation of drug release kinetics while preserving surface biocompatibility and therapeutic efficacy. The stability and long-term performance of PE-CVD coatings are critical for their function in biological environments. Studies have shown that PE-CVD-derived SiOx thin films exhibit superior hydrolytic stability compared with coatings produced by rapid thermal evaporation or conventional PVD, ensuring structural integrity during prolonged exposure to aqueous media. Such stability is essential for maintaining predictable diffusion barriers and preventing premature degradation of the drug delivery system. Beyond stability, plasma-polymerized films offer effective control over drug release behavior. Organosilicon plasma coatings, including those derived from tetramethylcyclotetrasiloxane, enable fine adjustment of release rates through precise control of film thickness and crosslinking density. By tuning these parameters, diffusion pathways can be modulated to accommodate different drug molecules and therapeutic requirements. Similarly, atmospheric-pressure plasma-deposited siloxane overlayers have been shown to markedly extend drug release durations, with reports of antibiotic release times increasing from hours to several days, highlighting the capacity of plasma coatings to sustain long-term therapeutic delivery.[97,98]

The absence of standardized frameworks for assessing the biocompatibility of plasma coatings deposited by PECVD represents a major bottleneck in the development of controlled drug release systems. This challenge largely stems from the wide diversity of plasma processes, precursor chemistries, and deposition conditions used to fabricate such coatings, all of which strongly influence surface chemistry and morphology. As a result, biocompatibility outcomes reported across studies are often difficult to compare, limiting reproducibility and hindering regulatory translation. A key contributor to this problem is the intrinsic variability of plasma coating techniques. Plasma-polymerized films used in drug delivery applications can exhibit substantial differences in crosslinking density, chemical functionality, and stability depending on plasma power, duty cycle, and precursor selection. These variations directly affect drug diffusion behavior and biological responses, complicating the establishment of uniform evaluation criteria. Moreover, distinct PECVD modalities, such as capacitively coupled plasma chemical vapor deposition and PACVD, generate coatings with fundamentally different physicochemical characteristics, further challenging attempts at standardization. Surface properties introduced by plasma coatings also play a decisive role in biocompatibility. Parameters such as surface roughness, porosity, and wettability significantly influence protein adsorption, cell adhesion, and cell viability. Since these features can vary widely between plasma-derived films, even when similar materials are used, biocompatibility assessments often need to be tailored to individual coating systems. In addition, variations in chemical composition such as the incorporation of bioactive elements or compounds, including titanium-containing carbonitride layers can enhance cellular responses but simultaneously necessitate customized testing strategies to accurately capture their biological effects. Compounding these issues is the lack of universally accepted biocompatibility testing protocols for plasma coatings. Differences in cell models, assay conditions, and evaluation endpoints frequently lead to inconsistent or non-comparable results across studies. This problem is further intensified in drug delivery systems, where the interaction between the coating and the encapsulated or released drug adds an additional layer of biological complexity. In such cases, both the surface–cell interface and the coating–drug interplay must be evaluated concurrently, underscoring the need for harmonized, application-specific standards to reliably assess the biocompatibility of PECVD-derived plasma coatings.[99,100]

Translational Benchmarking

To contextualize the translational readiness of PECVD coatings, Table 2 compares PECVD with commonly used barrier and drug-release materials, including parylene, polyurethane (PU), poly(lactic-co-glycolic acid) (PLGA), and ALD/iCVD-derived films. Attributes relevant to regulatory evaluation such as ISO 10993 biocompatibility endpoints, sterilization compatibility (ethylene oxide, gamma irradiation, e-beam), aging stability, extractables/leachables, and manufacturability are summarized to highlight relative advantages and limitations.

Future Perspectives and Clinical Translation

Future research on PECVD for biocompatible drug-release coatings needs to move from proof-of-concept films toward rigorously engineered, clinically validated platforms. PECVD offers precise control over film thickness, crosslinking density, chemistry, and porosity, which can be exploited to tune diffusion-controlled and stimuli-responsive release profiles on implants, stents, micro/nanoparticles, and transdermal systems. However, translation will require systematic mapping between plasma process parameters (precursor chemistry, power, duty cycle, pressure, gas composition) and pharmacokinetic outputs (lag time, burst suppression, zero-order or pulsatile release) under physiologically relevant conditions, including dynamic flow, protein adsorption, and mechanical loading. High-throughput experimental design, coupled with multiscale modelling of plasma–surface interactions and drug transport, could accelerate the establishment of robust design spaces that are transferable across devices and manufacturing sites. A critical perspective for clinical translation is long-term biocompatibility and stability of PECVD coatings in complex biological environments. Future studies should integrate standardized cytocompatibility, hemocompatibility, and immunocompatibility testing with accelerated ageing and real-time degradation assays in serum, synovial fluid, and other relevant media. Particular attention is needed for coatings intended for chronic intravascular or intracranial implants, where subtle changes in surface chemistry, crosslinking, or residual radicals may influence thrombosis, endothelialization, microglial activation, or glial scarring. Comparative in vivo studies that benchmark PECVD films against established polymer coatings (e.g., parylenes, PUs, PLGA) with respect to foreign-body response, fibrosis, and device integrity will be essential to convince regulators and clinicians of their added value. In parallel, the potential of PECVD to graft bioactive ligands, stealth hydrophilic layers, or antibacterial components in a single step should be systematically explored to create multifunctional "release + biointerface" coatings. From a manufacturing and regulatory standpoint, the scalability, reproducibility, and cost-effectiveness of PECVD processes must be demonstrated on clinically relevant devices. Future work should address conformal coating of complex 3D geometries (e.g., porous scaffolds, braided stents, microstructured catheters), compatibility with heat- or solvent-sensitive drug cargos, and integration with aseptic processing and sterilization workflows. Process analytical technologies and real-time plasma diagnostics could be deployed to enable closed-loop control of film properties and to generate the detailed process documentation required under Good Manufacturing Practice. Early engagement with regulatory agencies to define acceptable characterization panels covering chemistry, mechanical performance, extractables/leachables, and in vitro–in vivo correlation of drug release will help de-risk translation. Partnerships with device manufacturers can facilitate pilot clinical applications in niches where existing coatings are suboptimal, such as drug-eluting neurovascular devices, long-acting contraceptives, or implantable biosensors. Finally, future perspectives should emphasize convergence with precision medicine and smart drug-delivery paradigms. PECVD is uniquely positioned to generate coatings that respond to pH, redox state, enzymatic activity, or external triggers (light, electric field, ultrasound), enabling on-demand or feedback-controlled dosing tailored to individual patients. Coupling PECVD-modified surfaces with embedded sensors and wireless telemetry could create closed-loop systems where local drug release is adjusted in real time based on biomarker readouts or device performance. Integration of data-driven optimization using machine learning to relate plasma recipes, coating structure, and clinical endpoints may further accelerate iterative improvement and personalization. Overall, the clinical translation of PECVD-based biocompatible coatings will depend on coordinated advances in mechanistic understanding, safety and durability assessment, scalable manufacturing, and smart device integration, but the technology holds substantial promise to enable the next generation of controlled drug-release systems with improved efficacy, safety, and patient adherence (Figure 4).

Limitation

A major limitation arises from the wide variability in PECVD operating conditions across studies, including plasma power, duty cycle, pressure, gas composition, and deposition time. These parameters critically influence film chemistry, crosslinking density, and surface energy, yet they are rarely standardized or reported within comparable ranges. This heterogeneity precludes quantitative meta-analysis and limits the ability to establish universal process–structure–function relationships. Many studies provide incomplete or selective physicochemical characterization of coatings. While techniques such as XPS, FTIR, contact angle measurements, and porosity analysis are essential for mechanistic understanding, they are not uniformly applied. In several reports, key parameters such as coating thickness, chemical stability, and degradation kinetics are either missing or insufficiently described, reducing reproducibility and comparability.

Drug-release outcomes are reported using diverse and often non-overlapping metrics. Critical parameters such as initial burst release percentage, release rate constant (k), diffusion exponent (n), and time to 50% release (t_{50}%) are inconsistently quantified or entirely

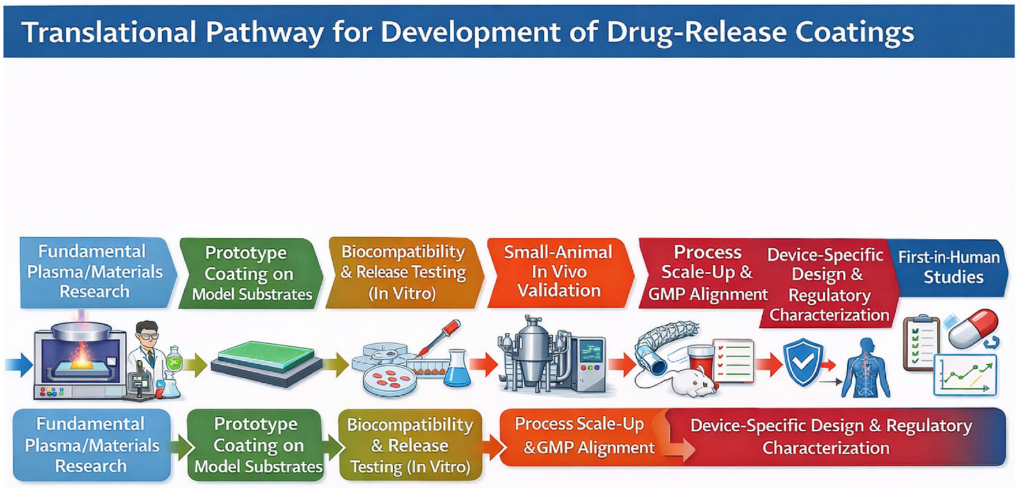

Fig 4 | The figure outlines the translational pathway for the development of drug-release coatings, progressing from fundamental plasma and materials research to clinical application. Initial studies focus on understanding plasma material interactions and fabricating prototype coatings on model substrates, followed by in vitro evaluation of biocompatibility and drug-release behavior. Promising systems are then advanced to small-animal in vivo validation to assess safety and therapeutic performance. Subsequent process scale-up with GMP alignment ensures manufacturing reproducibility and regulatory compliance, while device-specific design and regulatory characterization tailor the coating to its intended clinical use. This structured pathway ultimately enables first-in-human studies and supports the systematic translation of PECVD-based drug-delivery coatings from bench to bedside absent. This lack of standardized reporting complicates cross-study comparison and undermines robust evaluation of coating performance. The majority of included studies rely on in vitro release models or short-duration in vivo experiments. While these approaches are valuable for early-stage evaluation, they do not adequately capture long-term coating stability, chronic biocompatibility, immune responses, or device–tissue interactions under physiological conditions. Consequently, the translational relevance to implantable or long-term drug-delivery systems remains limited.

Several studies focus heavily on physicochemical properties and release profiles while providing minimal biological validation. Comprehensive evaluation of cell compatibility, inflammatory responses, endothelialization, thrombogenicity, or tissue integration is often lacking, particularly for cardiovascular or implantable applications. This imbalance constrains conclusions regarding true clinical suitability. Differences in substrate materials (e.g., metals, polymers, ceramics), device geometries, and drug classes introduce additional confounding factors. Plasma–surface interactions and coating performance can vary substantially with substrate chemistry and topology, making it difficult to generalize findings across different biomedical devices. As with many emerging technology fields, there is a likelihood of publication bias toward positive outcomes. Negative results, failed coatings, or suboptimal release behaviors are underreported, which may lead to an overestimation of PECVD efficacy and robustness. Additionally, language and database restrictions may have excluded relevant studies. Few studies address scalability, batch-to-batch reproducibility, sterilization compatibility, or regulatory considerations critical for clinical translation. Manufacturing challenges, cost-effectiveness, and compliance with regulatory standards (e.g., ISO, FDA) are rarely discussed, limiting practical applicability of the findings. The reviewed literature spans multiple decades during which PECVD technologies have evolved significantly. Earlier studies often use legacy plasma systems with limited control over parameters, whereas recent works employ advanced pulsed or atmospheric plasma platforms. This temporal variability complicates direct comparison and may bias conclusions toward older or less optimized methodologies.

Discussion

From a translational perspective, future PECVD drug-eluting devices should incorporate ISO 10993-guided biocompatibility testing, extractables and leachables assessments, and evaluation of sterilization (EtO, gamma, e-beam) and aging effects on plasma polymer films. Regulatory pathways for combination products under FDA and EMA frameworks should be considered early, with comparative benchmarking against incumbent coatings such as parylene, PU, and PLGA.

Conclusion

PECVD has emerged from this review as a versatile and highly tunable platform for engineering biocompatible coatings that enable sophisticated control over drug release from a wide range of medical devices and delivery systems. Across in vitro and in vivo studies, PECVD has been shown to generate conformal, pinhole-free films on complex geometries while allowing precise adjustment of chemistry, crosslink density, thickness, and porosity, thereby shaping diffusion, degradation, and stimuli-responsive release kinetics with a level of control that is difficult to achieve using conventional wet-chemical methods. Importantly, the technique can operate at relatively low substrate temperatures and in dry conditions, making it compatible with heat- and solvent-sensitive drug cargos and polymeric substrates commonly used in implantable and transdermal formulations. At the same time, this review highlights that PECVD-based systems are not yet fully mature for broad clinical deployment. Many studies rely on simplified model drugs, static release conditions, and short test durations, which may underestimate the impact of protein adsorption, mechanical stresses, and long-term degradation in vivo. Biocompatibility data are encouraging but remain fragmented, with limited systematic assessment of chronic inflammation, thrombogenicity, and immune responses for specific chemistries and device contexts. Furthermore, process descriptions are often insufficiently detailed to ensure reproducibility across laboratories or scaling to industrial settings, and formal correlations between plasma parameters, film structure, and pharmacokinetic performance are still incompletely developed. These gaps collectively underscore that PECVD's demonstrated capabilities in surface engineering have yet to be fully translated into robust, regulatory-ready drug-release products.

Overall, the evidence synthesized in this review supports PECVD as a powerful enabling technology rather than a single, monolithic solution: its true value lies in the capacity to integrate multiple functions-controlled release, bioinert or bioactive interfaces, antifouling or antimicrobial properties within a single, conformal coating architecture. Realizing this potential will require coordinated efforts to standardize plasma process reporting, strengthen long-term biocompatibility and stability data, and embed PECVD development within quality-by-design and Good Manufacturing Practice frameworks aligned with regulatory expectations for combination products. If these challenges are systematically addressed, PECVD-derived biocompatible coatings are well positioned to underpin the next generation of controlled drug-release systems ranging from drug-eluting stents and orthopedic implants to implantable biosensors and micro/nanocarriers offering improved therapeutic precision, safety, and patient adherence in diverse clinical settings.

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