

Review

Not peer-reviewed version

Pharmaceutical Packaging Materials and Medication Safety: A Mini-Review

[Yaokang Lv](#)^{*}, Nianyu Liu, Chao Chen, [Zhiwei Cai](#), Jianhang Li

Posted Date: 6 May 2025

doi: 10.20944/preprints202505.0119.v1

Keywords: medication safety; pharmaceutical packaging; contamination; barrier; nanomaterials; intelligent packaging



Preprints.org is a free multidisciplinary platform providing preprint service that is dedicated to making early versions of research outputs permanently available and citable. Preprints posted at Preprints.org appear in Web of Science, Crossref, Google Scholar, Scilit, Europe PMC.

Copyright: This open access article is published under a Creative Commons CC BY 4.0 license, which permit the free download, distribution, and reuse, provided that the author and preprint are cited in any reuse.

Review

Pharmaceutical Packaging Materials and Medication Safety: A Mini-Review

Yaokang Lv ^{1,*}, Nianyu Liu ¹, Chao Chen ², Zhiwei Cai ² and Jianhang Li ³

¹ College of Chemical Engineering, Zhejiang University of Technology, Hangzhou, 310014, China

² Zhejiang Institute for Food and Drug Control, Hangzhou, 310052, China

³ Hangzhou Plastics Industry Co., Ltd., Hangzhou, 311300, China

* Correspondence: yaokanglv@zjut.edu.cn

Abstract: Pharmaceutical packaging materials play a crucial role in ensuring the safety and efficacy of medications. Common materials include glass, plastics, metals, and rubber, each with unique properties. However, risks such as migration, microbial contamination, and poor barrier performance may compromise medication safety. This review summarizes the impact of packaging materials on medication safety, discusses recent regulatory updates in China, and highlights research progress and emerging technologies like nanomaterials, green packaging materials and intelligent packaging that may offer new opportunities for pharmaceutical industry.

Keywords: medication safety; pharmaceutical packaging; contamination; barrier; nanomaterials; intelligent packaging

1. Introduction

Pharmaceutical packaging is an indispensable part of drugs, consisting of a collection of packaging components made from various materials [1]. It plays a crucial role in the entire process from drug production to patient use, ensuring the safety, adaptability, stability, functionality, protection, and convenience of drugs [2]. The various types of packaging materials, including glass, plastics, metals, and rubber, each have unique properties. Glass has good chemical stability and is generally used for packaging injectable drugs; plastics have good processing properties and are cost-effective, widely used in various pharmaceutical packaging; metal containers have high strength and are suitable for packaging aerosols and other pressurized products; Rubber plays a key role in sealing applications such as bottle caps and stoppers [3]. During drug packaging, many key factors must be fully considered, with patient safety being the primary principle [4,5]. Ensuring that drug efficacy does not deviate and maintaining consistent drug quality are core requirements. Strict supervision of packaging material components and production processes is necessary to prevent drug contamination and deterioration, effectively limiting microbial contamination, which plays a key role in maintaining drug safety and effectiveness [6–8].

Pharmaceutical packaging materials may have a significant impact on medication safety. From a physical performance perspective, if the barrier properties are poor, oxygen, moisture, and light can enter the packaging, causing the drug quality to deteriorate. For example, vitamin C is easily oxidized, aspirin is prone to hydrolysis, and chlorpromazine is susceptible to photochemical reactions. If the mechanical performance is poor, such as insufficient strength, toughness, and elasticity of the packaging material, it may cause damage, leakage, or deterioration of drugs during production, transportation, and storage. From a chemical performance perspective, migration phenomena can cause additives or components from the packaging material to migrate into the drug, affecting its quality and safety. For example, plasticizers in PVC infusion bags can migrate, and glass packaging materials can release alkaline substances. Adsorption can cause insufficient drug content and changes in properties, affecting efficacy and stability. Microbial contamination risk is particularly

evident in the production stage of packaging materials. Production environment, equipment, and process conditions, as well as the hygiene habits of operators, can all cause microbial contamination, posing a threat to drug quality and user health. With the steady progress of science and technology, the application of new materials in pharmaceutical packaging has attracted increasing attention. Nanomaterials, with their unique properties such as high specific surface area, excellent UV blocking effect, and antibacterial effect, have opened up new development opportunities for pharmaceutical packaging [9]. Intelligent packaging materials, with the help of modern science and technology, have realized functions such as self-inspection of drug quality, anti-counterfeiting, and measurement, optimizing the safety and convenience of drug circulation and use. Green packaging materials, with their characteristics of environmental protection, safety, and biodegradability, have become a key direction for the sustainable development of the pharmaceutical packaging industry. In-depth research on the relationship between pharmaceutical packaging materials and medication safety is of great significance in improving drug quality, ensuring patient medication safety, and promoting the development of the pharmaceutical packaging industry [10].

In this mini-review, the key aspects of pharmaceutical packaging materials and their impact on medication safety were summarized, the recent regulatory and research progress of pharmaceutical packaging materials in China were discussed, and emerging materials that may offer new opportunities for pharmaceutical industry were explored.

2. Classification of Pharmaceutical Packaging

The primary purpose of pharmaceutical packaging is to protect the product from all external factors. For instance, it safeguards medications from physical shocks such as vibration and friction to prevent impact damage, while also shielding them from environmental variations to avoid contamination by biological pollutants like mold, yeast, and bacteria. Pharmaceutical packaging also provides consumers with critical information about the medication, including usage instructions, side effects, warnings, manufacturer details, and pricing. Additionally, companies often use bold colors, logos, and symbols on pharmaceutical packaging to stand out from competitors and promote their products, aiming to influence purchasing decisions [11–44]. To achieve these objectives, pharmaceutical packaging is generally divided into external packing and immediate packaging [46–48].

2.1. External Packing

Pharmaceutical external packaging plays a crucial role throughout the entire process from drug production to actual use. During transportation, medications usually face diverse and complex environments with potential risks: collisions during loading/unloading, vibrations from vehicle movement and environmental humidity. For example, injectable medications in glass vials could easily shatter during transit without the protection of boxes, leading to spillage, waste, and delayed treatment [45], while as a kind of external packaging, sturdy corrugated boxes provide cushioning effects, reducing external forces and preventing breakage, deformation, or damage caused by vibrations. Humidity is also a key factor affecting drug quality, hygroscopic medications, such as granules or powders, may clump or develop mold when exposed to humidity, reducing efficacy or even generating harmful substances that endanger patient safety. Cartons and boxes with moisture-resistant properties effectively block dampness, preventing moisture-induced degradation [46].

Maintaining the integrity of external packaging is important during manufacturing, transportation and storage. Manufacturers must use high-quality, standardized materials to ensure cartons and boxes possess robust moisture and shock resistance. Transport personnel should handle packages with care to avoid sharp impacts. Storage facilities must monitor environmental conditions, regularly inspect packaging for damage, and address issues promptly. By prioritizing these measures, the protective functions of external packaging are fully realized, ensuring effective medication use and safeguarding patient safety [47].

2.2. Immediate Packing

Immediate packing, such as ampoule bottles, vials, and medicinal pouches, is critically linked to drug quality and safety. Immediate packing materials form the 'first line of defense' for pharmaceutical integrity. Ampoule bottles, typically made of hard borosilicate glass, offer excellent chemical stability and hermetic sealing to block air, moisture, and microorganisms, ensuring sterile storage. Vials often utilize borosilicate glass for its thermal shock resistance and chemical inertness, making them ideal for lyophilized drugs and injectables. Medicinal pouches are commonly fabricated from polymers like polyethylene or polypropylene, whose physicochemical properties (e.g., gas permeability, moisture resistance, and corrosion resistance) directly determine drug shelf life and stability.

Even minor material defects of immediate packing can significantly compromise drug quality. For instance, inadequate microbial barrier properties in pouches may allow pathogen infiltration during storage, leading to contamination, reduced efficacy, and severe patient health risks. Consequently, such packaging materials must undergo rigorous quality testing and safety evaluations during production and application to ensure pharmaceutical safety [48].

3. Common Pharmaceutical Packaging Materials

Common pharmaceutical packaging materials include the following categories:

3.1. Glass

Glass belongs to the non-crystalline amorphous fused solid that does not crystallize under rigid cooling conditions [12–14]. Glass pharmaceutical packaging materials, owing to their excellent physicochemical properties, have become the most important pharmaceutical packaging materials with the longest application history and the widest application range in China [14]. The United States Pharmacopeia (USP) and European Pharmacopoeia (EP) also specifically recognize two types of glass for safe parenteral drug packaging: Type I borosilicate glass and Type II soda-lime glass. Ampoule bottles normally made of borosilicate glass or soda - lime glass, but vials commonly made of borosilicate glass [12].

Chemical durability is a critical property of pharmaceutical glass, where borosilicate glass outperforms soda-lime glass. The typical chemical composition of borosilicate glass is as follows: silicon dioxide (SiO_2) accounts for 70.00 ~ 80.00 wt%, boric anhydride (B_2O_3) accounts for 7.00 ~ 13.00 wt%, sodium oxide (Na_2O) or potassium oxide (K_2O) accounts for 4.00 ~ 8.00 wt%, and aluminum oxide (Al_2O_3) accounts for 2.00 ~ 8.00 wt%. Borosilicate glass, which can be sterilized before and after filling, exhibits exceptional properties: high hydrolytic resistance, superior chemical durability and inertness, excellent thermal shock resistance and ultra-low thermal expansion coefficient. Therefore, this material has been widely used for sensitive drugs requiring stringent packaging, such as parenteral medications and blood products [13].

3.2. Metals

Metals for pharmaceutical packaging commonly refer to containers made from various metallic materials (including metallic coatings and alloys) used for packaging pharmaceuticals. In practical applications, they are primarily categorized into two types based on the base material: aluminum and its alloys, and stainless steel containers. Depending on whether internal surface treatment is applied, they can be classified as containers with inner coatings/platings or bare metal containers. These metal containers are suitable for packaging aerosols, sprays, ointments, and other formulations, given the wide variety of involved dosage forms, quality control of metals has received significant attention [15]. Elemental impurities introduced through raw materials or residual from manufacturing processes may leach into pharmaceuticals during storage, potentially affecting drug quality and safety. Aluminum is widely used in pharmaceutical packaging, especially in the form of aluminum foil. Aluminum foil is used for blister packaging of solid dosage forms [16]. It provides a good barrier against light, moisture, and oxygen, protecting the drugs from degradation. For

example, many tablets and capsules are packaged in blister packs with an aluminum foil backing [17].

3.3. *Plastics*

As synthetic polymers, plastic materials have largely replaced inorganic materials such as metal and glass in pharmaceutical packaging due to their flexibility, low cost, and ease of production. Polyethylene (PE), polypropylene (PP) and polyvinyl chloride (PVC) are well-known plastic materials used in pharmaceutical packaging. PE exhibits good flexibility, allowing it to conform to various drug shapes, along with excellent chemical stability—rarely reacting chemically with pharmaceuticals. It also processes well, enabling the production of diverse packaging containers [21,22]. PP offers high transparency, facilitating visual inspection of medications, and outstanding heat resistance, making it suitable for sterilization processes. It is durable, chemically stable, and widely used in pharmaceutical packaging [23,24]. PVC is flexible, transparent, and excels in heat-sealing performance, ensuring rapid and secure packaging closure [25,26]. Despite their advantages, plastics also present significant drawbacks such as plasticizer migration. During production, plasticizers are often added to plastic materials like PVC, which may further migrate into medications, posing health risks, especially affecting children’s endocrine and reproductive development. Additionally, broken plastic packaging fragments could be ingested by children, causing harm. To ensure medication safety, rigorous screening of plastic materials is essential for pediatric drug packaging [27,28].

On the other hand, compared to glass and metal, most plastic materials exhibit inferior barrier properties, allowing gradual permeation of oxygen and moisture that can compromise drug stability. To address this, plastics with enhanced barrier performance have been developed. Commonly used barrier materials in pharmaceutical packaging include polyvinylidene chloride (PVDC), ethylene-vinyl alcohol copolymer (EVOH), and polyvinyl alcohol (PVA). The barrier properties of typical plastic packaging materials are summarized in Table 1.

Table 1. Barrier performances of typical plastic packaging materials.

Type of plastics	O ₂ (cm ³ /m ² ·day) ¹	N ₂ (cm ³ /m ² ·day) ¹	CO ₂ (g/ m ² ·day) ²	H ₂ O vapor (g/ m ² ·day) ²
PVDC	4~10	0.1~0.8	0.3~0.7	0.4~1.0
(Polyamide)PA6	35	-	43~59	93~155
PP	300	60	1200	3.6~10.2
PVA	0.1~1	0.05~0.5	0.2~0.4	300~400
(Polyethylene terephthalate)PET	74~138	12~24	35~50	27.4~46.7
PVC	77~310	-	140~400	13.2~71.3
(Low density polyethylene)LDPE	500~700	200~400	2000~4000	15.2~23.4
(High density polyethylene)HDPE	200~500	13~300	2000~4000	3.5~11.1
(Polystyrene)PS	600~800	40~50	2000~4000	10.5~33.6
(Polyacrylonitrile)PAN	11.6	-	6	31~47.2
EVOH (32% ethylene)	0.2	0.02	0.9	47
EVOH (44% ethylene)	1.8	0.13	1.4	95

¹ Tested under 23 °C; ² Tested under 38 °C.

3.4. *Rubbers*

Rubbers are a kind of polymers that renowned for its exceptional elasticity, is an indispensable component of pharmaceutical packaging systems. Its quality and safety have always been focal points of industry attention. Rubber materials are commonly used in critical components such as

bottle caps and stoppers, where they form tight seals with container openings. This creates a reliable barrier against external moisture, oxygen, and microorganisms, ensuring the stability of pharmaceuticals during storage and transportation [29–44].

Elastomeric rubber stoppers play a unique role in pharmaceutical packaging as core primary packaging components for numerous sealed container systems. They serve not only as sealing closures for vials and syringes but also as plunger tips (pistons) in pre-filled syringes or cartridge-based systems. Elastomeric materials possess distinctive mechanical properties, enabling smooth penetration by hypodermic needles without bending or dulling them. They require minimal insertion force while rapidly regaining elasticity post-withdrawal to maintain a secure seal, preserving the integrity of the packaging system [42,43]. Currently, halogenated butyl rubber stoppers (primarily chlorinated and brominated butyl rubber) dominate applications for injectables, inhalants, and liquid formulations due to their low gas/moisture permeability, high chemical stability, heat/aging resistance, and superior self-sealing capabilities [30].

From a manufacturing perspective, most rubbers are produced by vulcanizing raw rubber to form crosslinked network structures. This vulcanization process imparts high strength and corrosion resistance, enabling vulcanized rubber to undergo significant deformation under stress while rapidly recovering its original shape post-stress removal. Sulfur, the earliest vulcanizing agent, faces limitations in butyl rubber applications. When exceeding its saturation solubility in butyl rubber stoppers, sulfur causes a "blooming" phenomenon that disrupts material homogeneity and compromises drug quality. Thus, stringent sulfur content monitoring has become a critical quality control parameter [36]. Nowadays, high-performance liquid chromatography (HPLC) is the standard method for detecting sulfur levels in halogenated butyl rubber stoppers, enabling precise quality risk mitigation [37–40].

Nevertheless, rubber materials present ongoing challenges. Issues such as permeability, adsorption tendencies, extractables, and release of subvisible particles require advanced solutions to ensure packaging quality and medication safety [43,44].

3. Impact on Medication Safety

3.1. Barrier Performances

Barrier properties of pharmaceutical packaging materials against oxygen, water vapor, and light play crucial roles in ensuring medication quality and safety [49]. Suboptimal barrier performance of packaging materials may lead to reduced efficacy and increased impurities in drugs, and significant threats to medication safety. Selecting appropriate packaging materials is therefore essential for maintaining drug quality. For example, vitamin C exhibits strong reducing properties and is prone to oxidation. If ordinary plastic bottles are used as packaging, oxygen can easily penetrate the plastic and oxidize vitamin C into dehydroascorbic acid, which further decomposes into products such as 2,3-diketogulonic acid. Prolonged consumption of deteriorated vitamin C tablets will not only fails to deliver the intended benefits of vitamin C supplementation but may also introduce harmful impurities, adversely affecting health. Therefore, good oxygen-resistant packaging is necessary to protect vitamin C tablets [50]. In humid environments, aspirin is susceptible to hydrolysis, generating salicylic acid and acetic acid. If the packaging material has weak water vapor barrier capabilities, moisture ingress can cause enteric-coated aspirin tablets to absorb humidity, accelerating hydrolysis reaction. moisture ingress can cause enteric-coated aspirin tablets to absorb humidity, accelerating hydrolysis [51]. Light-blocking performance is equally important. For instance, chlorpromazine tablets are photosensitive [52]. If transparent packaging is used in a light-exposed environment, chlorpromazine will undergo a series of photochemical reactions [53,54], decomposing into toxic free radicals and other products. This not only renders the drug ineffective but may also cause serious adverse reactions, such as skin allergies [55], liver damage and so on [55,56]:

3.2. Mechanical Performance

The mechanical properties of pharmaceutical packaging materials also profoundly impact medication safety [57]. Firstly, packaging materials must possess sufficient compressive, tensile, and impact resistance capabilities [58–61]. During production, transportation and storage, pharmaceuticals inevitably endure external forces such as stacking, collisions, and vibrations [62]. Excessively thin packaging boxes may collapse under stacking pressure, causing internal medications to break or deform, compromising drug efficacy. Plastic bottles with inadequate rigidity may crack upon minor impacts, leading to drug leakage, cross-contamination, and posing risks to patient health [63]. Secondly, pharmaceutical packaging materials should demonstrate appropriate toughness [64]. For example, pharmaceutical blister packaging requires plastic materials with excellent toughness to securely encapsulate medications while protecting tablets or capsules from damage through deformation when compressed [65]. Additionally, elasticity of packaging materials is also related to medication safety [66]. For instance, flexible tubes for topical ointments must maintain elasticity to ensure smooth extrusion and preserve airtightness after repeated compression. This prevents air ingress that could oxidize and degrade the ointment, thereby ensuring safe usage and storage [67].

3.3. Migration Phenomenon

The migration phenomenon in pharmaceutical packaging materials poses significant risks to medication safety [68]. During the production of plastic, rubber, and other packaging materials, various additives such as plasticizers, stabilizers, and antioxidants are incorporated to enhance material performance. However, during the storage of pharmaceuticals, these additives may migrate from the packaging materials into the drugs [69]. Di(2-ethylhexyl)phthalate (DEHP), a plasticizer, may be added to PVC infusion bags. But if DEHP migrates into the human body, it may interfere with the endocrine system, hinder reproductive development, and pose greater risks to sensitive populations such as infants and pregnant women [70]. Beyond additives, migration of intrinsic packaging components can also occur. Certain glass packaging materials, when in contact with aqueous solutions like injectables, may release alkaline substances or insoluble flakes. This not only alters the pH of medications but also introduces particulate contamination. If such particles enter the bloodstream, they increase the risk of thrombosis [71]. In addition, interactions between highly oxidizing drugs and reducing packaging materials may trigger redox reactions. This can degrade drug efficacy or generate toxic substances, severely compromising patient safety [20]. Therefore, rigorously controlling the chemical properties of pharmaceutical packaging materials and preventing migration-related hazards are critical to safeguarding medication safety.

3.4. Adsorption Effect

Adsorption in pharmaceutical packaging poses critical safety risks. Many plastic and rubber packaging materials adsorb fat-soluble drugs, volatile compounds, or active ingredients. For example, antibiotics in plastic bottles may lose potency as packaging adsorbs active ingredients, leading to underdosing and delayed treatment [73]. Protein-based biologics stored in rubber-sealed vials risk structural changes if rubber adsorbs proteins, which reduces efficacy and may trigger allergic reactions due to immunogenic byproducts [74,75]. Plastic films adsorbing drug volatiles can become brittle, compromising seal integrity and accelerating drug degradation [76]. Since adsorption impacts drug potency, stability, and packaging performance, selecting low-adsorption materials is vital for medication safety.

3.5. Microbial Contamination Risk

During the production of pharmaceutical packaging, microbial contamination is one of the key factors affecting pharmaceutical safety [77]. If the manufacturing environment fails to meet required cleanliness standards, microbial (such as bacteria, fungi and viruses) growth becomes highly likely [78]. For instance, in facilities producing paper-based packaging materials, improper humidity control or inadequate sanitation can lead to excessive proliferation of mold and other

microorganisms. Even if contaminated paper is used for outer packaging without direct contact with medications, microbes may migrate into the drugs through gaps or pores during storage or transportation, jeopardizing product quality [79]. Production equipment and processes also contribute to microbial contamination. During plastic packaging manufacturing, residual microbes may adhere to surfaces if machinery like injection molding machines is not regularly cleaned and sterilized. For plastic bottles directly contacting medications, bacterial contamination during production can lead to microbial growth post-filling, causing drug degradation, loss of efficacy, or even user infections. The hygiene practices of operators are equally important. Inadequate handwashing by workers may introduce pathogenic microbes such as *Escherichia coli* or *Staphylococcus aureus* to packaging materials. This risk is especially acute for components like injection vial stoppers or eye-drop dispensers that directly contact medications. Even trace microbial contamination in such parts can render drugs unsafe, posing severe health risks to users [80]. Therefore, strict control across all production stages of pharmaceutical packaging materials, particularly manufacturing environments, is essential to eliminate microbial contamination and safeguard pharmaceutical safety.

Currently in China, pharmaceutical packaging material manufacturers are required to establish cleanrooms based on the intended use and characteristics of the materials, with cleanliness levels corresponding to those of the drug production environments they serve. Regulatory authorities are mandated to inspect and validate the performance parameters of these cleanrooms, with testing methods aligned to referenced standards such as those outlined in Table 2.

Table 2. Detection items, methods and standard for cleanrooms.

Detection Items	Detection Methods	Detection Standard
Temperature (°C)	Code for Construction and Acceptance of	18 - 26 °C (or adapted to the production process)
Relative Humidity (%)	Cleanrooms (GB 50591—2010)	45% - 65% (or adapted to the production process)
Static Pressure Difference (Pa)		To the outside: ≥ 10 Between different cleanliness levels: ≥ 10 To non - clean areas: ≥ 10
Air Change Rate (times/h)		D - class: ≥ 20
Illuminance (lx)		Main workrooms > 300, other workrooms > 150
Maximum Permissible Number of Dust Particles (particles/m ³)	Test Methods for Floating Bacteria and Settling Bacteria in Cleanrooms (Areas) of	D - class: ≥ 0.5 μm, 3520000 particles; ≥ 5 μm, 29000 particles
Maximum Permissible Number of Microorganisms (pieces/m ³ or pieces/dish)	Pharmaceutical Industry (GB/T 16293 - 16294—2010)	D - class: - Floating bacteria: 200 (CFU/m ³) - Settling bacteria: 100 (Φ90 mm petri dish, CFU/4 h)

3.5. Standards for Pharmaceutical Packaging Materials

Owing to the significant impact of pharmaceutical packaging materials on medication safety, the production, processing, and use of all pharmaceutical packaging materials must strictly comply

with the regulations and standards established by regulatory authorities [81–84]. USP serves as the comprehensive standard for drug quality control in the United States. Compiled by the United States Pharmacopeial Convention, it provides the legal basis for the production, use, and regulatory testing of pharmaceuticals in the country. As shown in Table A1, the USP-NF-2023 edition includes extensive and highly detailed requirements for pharmaceutical packaging materials. EP edited and published by the European Directorate for the Quality of Medicines & HealthCare (EDQM), saw its 11th edition (EP 11.0) come into effect in January 2023. EP 11.0 is currently the sole authoritative guideline for pharmaceutical quality testing in Europe. All manufacturers must comply with its quality standards when marketing and using pharmaceutical products within the European region. Table A2 illustrates that the sections on pharmaceutical packaging materials in EP 11.0 are divided into two main parts: "3.1 Materials for Containers for Manufacturing" and "3.2 Containers." The Japanese Pharmacopoeia (JP) is developed by the Japanese Pharmacopoeia Editorial Committee and enforced by the Japanese Ministry of Health, Labour and Welfare. The latest edition, JP 18, became effective in 2021. As indicated in Table A3, JP 18 provides relatively concise guidelines for pharmaceutical packaging materials, with a specific focus on containers for injectable formulations.

In 2015, the Chinese Pharmacopoeia Commission published the 2015 Edition of the National Standard for Pharmaceutical Packaging Materials, which comprehensively covers packaging materials for all dosage forms used in China’s pharmaceutical industry. The Pharmacopoeia of the People’s Republic of China (ChP) 2020, also compiled and promulgated by the Chinese Pharmacopoeia Commission, dedicates 18 chapters to pharmaceutical packaging materials (Table 3). Unlike USP-NF-2023, which serves as a reference standard, both the National Standard for Pharmaceutical Packaging Materials and ChP 2020 are legally mandatory standards in China.

Table 3. ChP 2020 pharmaceutical packaging material standard system.

Type of standard	Number	Name of standard
Testing methods for glass containers	<4001>	Determination method for water resistance of glass particles at 121 °C
Material identification testing methods	<4002>	Packaging materials - Infrared spectroscopic determination method
Testing methods for glass containers	<4003>	Glass internal stress determination method
Mechanical performance testing methods	<4004>	Peel strength determination method
Mechanical performance testing methods	<4005>	Tensile testing method
Testing methods for glass containers	<4006>	Method for determination of internal surface water resistance
Barrier performance testing methods	<4007>	Gas permeability measurement method
Mechanical performance testing methods	<4008>	Thermal strength determination method
Testing methods for glass containers	<4009>	Boron trioxide determination method
Barrier performance testing methods	<4010>	Determination method for water vapor permeability
Biosafety testing methods	<4011>	Acute systemic toxicity test method for drug packaging materials
Material identification testing methods	<4012>	Method for determining the density of pharmaceutical packaging materials

Biosafety testing methods	<4013>	Hemolysis test method for drug packaging materials
Biosafety testing methods	<4014>	Cell toxicity testing method for drug packaging materials
Mechanical performance testing methods	<4015>	Test method for puncture force of rubber stoppers and gaskets for injection
Mechanical performance testing methods	<4016>	Determination method for puncture debris of injection plugs and gaskets
guiding principle	<9621>	Guiding principles for general requirements of pharmaceutical packaging materials
guiding principle	<9622>	Guidelines for Medicinal Glass Materials and Containers

4. Novel Materials for Pharmaceutical Packaging

4.1. Nanomaterials

Recent studies have shown that nanomaterials, leveraging their unique physicochemical properties—particularly their high specific surface area—have become critical elements for optimizing process efficiency and enhancing the comprehensive performance of materials. As next-generation UV-blocking composite materials, nanocomposite films demonstrate significant potential in pharmaceutical packaging and storage. By effectively blocking ultraviolet radiation, they prevent drug degradation and deterioration caused by light exposure, thereby ensuring drug quality and safety [85–89]. Rukmanikrishnan B. et al. incorporated zinc oxide nanoparticles (NPs) into gellan and xanthan gum nanocomposite films, significantly improving their glass transition temperature, thermal stability as well as tensile strength. These new nanocomposite films may be suitable for pharmaceutical packaging applications [86]. As shown in Figure 1, Patil, A. S. et al. successfully fabricated a flexible, highly transparent, and re-emissive PVA/waste tea residue carbon dots (PVA@WTR-CDs) composite thin films through solvent casting method. Their research confirmed that higher concentrations of WTR-CDs in PVA films enhance UV-blocking capabilities, achieving 100% UV-C (230–280 nm) and UV-B (280–315 nm) blocking, along with 20%–60% blocking in the UV-A (315–400 nm) region. PVA@WTR-CDs can be used as a modern UV blocking material in pharmaceutical storage, packaging and coating [87]. Razali, M.H. et al. developed bionanocomposite films based on gellan gum and TiO2 nanotube. These new bionanocomposite films not only exhibit high tensile strength and young modulus but also display strong antibacterial activity against pathogens such as Escherichia coli, Streptococcus, Pseudomonas aeruginosa and Staphylococcus aureus, which may also make a beneficial contribution to pharmaceutical packaging [88].

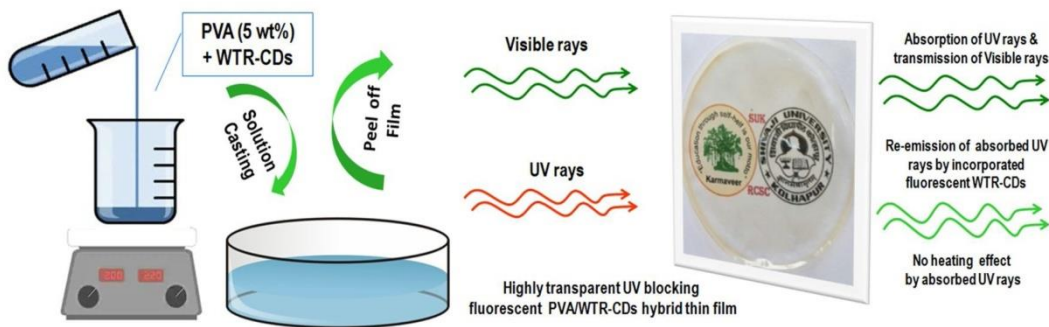


Figure 1. Schematic for fabrication of PVA@WTR-CDs composite thin films and their UV blocking applications [87].

4.2. Intelligent Packaging Materials

Intelligent pharmaceutical packaging materials and smart packaging encompass various categories such as information technology-based, active material-based, and structurally protective types. These innovations represent interdisciplinary achievements integrating computer science, materials science, artificial intelligence, industrial design, modern control theory, and microelectronics. The novel packaging materials and their derivative functions not only significantly enhance management efficiency and information collection capabilities in pharmaceutical logistics but also provide consumers with safe and convenient medication protection through comprehensive safety design and functional implementation. They have become frontier directions for global pharmaceutical packaging exploration and development [90–100].

Child Resistant Packaging (CRP), a typical example of structurally protective smart packaging, effectively prevents unauthorized opening by children through its special safety cap locking mechanism design. This design balances safety and convenience by avoiding accidental medication ingestion while maintaining accessibility for adults [99]. Furthermore, RFID technology offers efficient solutions for wireless measurement of environmental parameters. By enabling real-time monitoring of temperature, humidity, and light intensity, it provides timely warnings for abnormal conditions, preventing drug deterioration caused by unsuitable environments and ensuring pharmaceutical quality at the source [90–92]. As shown in Figure 2, Yang, G. et al. developed an intelligent medication packaging system (iMedPack) featuring RFID-enabled communication capabilities and functional material-driven actuation [93]. RFID technology also enables unified identification, anti-counterfeiting, traceability, and tamper resistance for pharmaceuticals. This not only reduces production and distribution costs while minimizing waste and shortening delivery time, but also enables precise drug tracking to prevent counterfeit products from entering the market [94]. In anti-counterfeiting innovation, intelligent pharmaceutical packaging materials demonstrate unique advantages. Some packaging utilizes special inks to print hidden patterns and texts that only reveal distinct colors under ultraviolet or infrared light, creating difficult-to-replicate anti-counterfeiting identifiers. This technology effectively combats counterfeit drug production and distribution, safeguarding consumer medication safety [95]. Leem J.W. et al. developed edible and scalable matrix codes using fluorescent silk fibroin, which can serve as labels for pharmaceutical information representation and data storage. These codes enable drug serialization, tracking, tracing, and authentication, enhancing pharmaceutical security and combating illegal drugs [96].

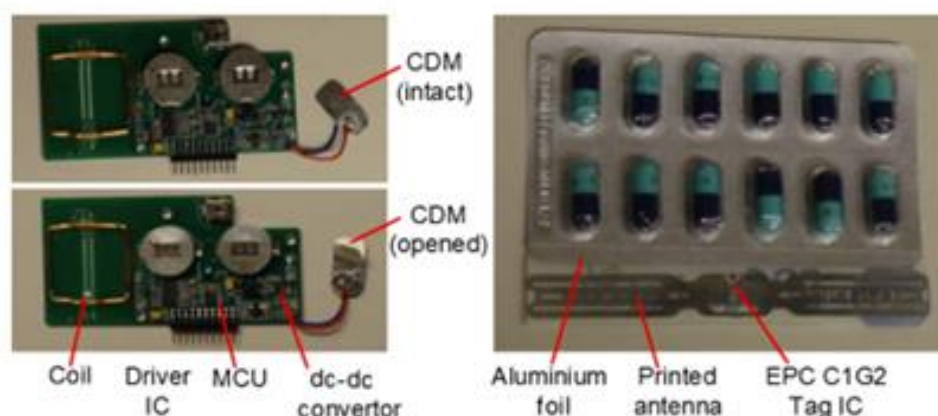


Figure 2. Examples of an iMedPack prototype [93].

4.3. Green Packaging Materials

Microbial Green packaging materials refer to environmentally friendly packaging solutions that pose no harm to human health and ecosystems throughout their entire lifecycle—from production and use to disposal. Primarily composed of natural bio-based polymers, these materials ensure pharmaceutical safety during packaging, transportation, and storage due to their excellent mechanical properties and biocompatibility. Their non-toxic nature eliminates contamination risks from harmful substances in packaging materials, while their biodegradability significantly reduces long-term environmental pollution caused by traditional packaging waste [101–116]. With rising global environmental awareness and sustainability priorities, the development and application of green packaging materials have gained international momentum. Worldwide governments are implementing supportive policies, including financial subsidies and tax incentives, to promote industry growth. Concurrent advancements in production technologies have enabled green packaging materials to match or surpass conventional materials in critical properties such as strength, toughness, and barrier performance [102].

As shown in Figure 3, Mohammadi, S. et al. developed a biodegradable PVA/CS/GO-PEG films by incorporating graphene oxide-polyethylene glycol nanohybrids (GO-PEG) into a polyvinyl alcohol/chitosan-carbohydrate (PVA/CS) blend. This material exhibits enhanced glass transition temperature (T_g), Young's modulus, tensile strength, elongation at break, and antimicrobial properties, positioning it as a promising candidate for drug packaging [103]. Nanocellulose materials derived from plant cellulose (e.g., cotton, bamboo, wheat, rice, sugarcane) not only improve mechanical and barrier performance of packaging—effectively preventing moisture damage and drug degradation during storage—but also offer cost-effectiveness, making them ideal for balancing safety and affordability in pharmaceutical applications. This innovation has attracted significant academic and industrial interest [104]. Yuan, C. et al. systematically analyzed structural properties and applications of biodegradable plastics, highlighting polybutylene succinate (PBS) as a safe, eco-friendly option for pharmaceutical outer packaging. Although PBS is not bio-based, its biodegradability avoids the persistent environmental hazards associated with traditional plastic waste [105]. In green composite research, polylactic acid-based composites have gained prominence for their high performance. Incorporating natural fibers as reinforcements further enhances packaging strength and stability, better protecting pharmaceuticals during transit [106,107]. Plant-based natural fibers such as sisal, jute, cotton, coir, and bamboo are now widely used in biocomposite packaging across industries. These materials combine robust physical properties with inherent non-toxicity, providing multi-layered safety assurances for pharmaceutical packaging

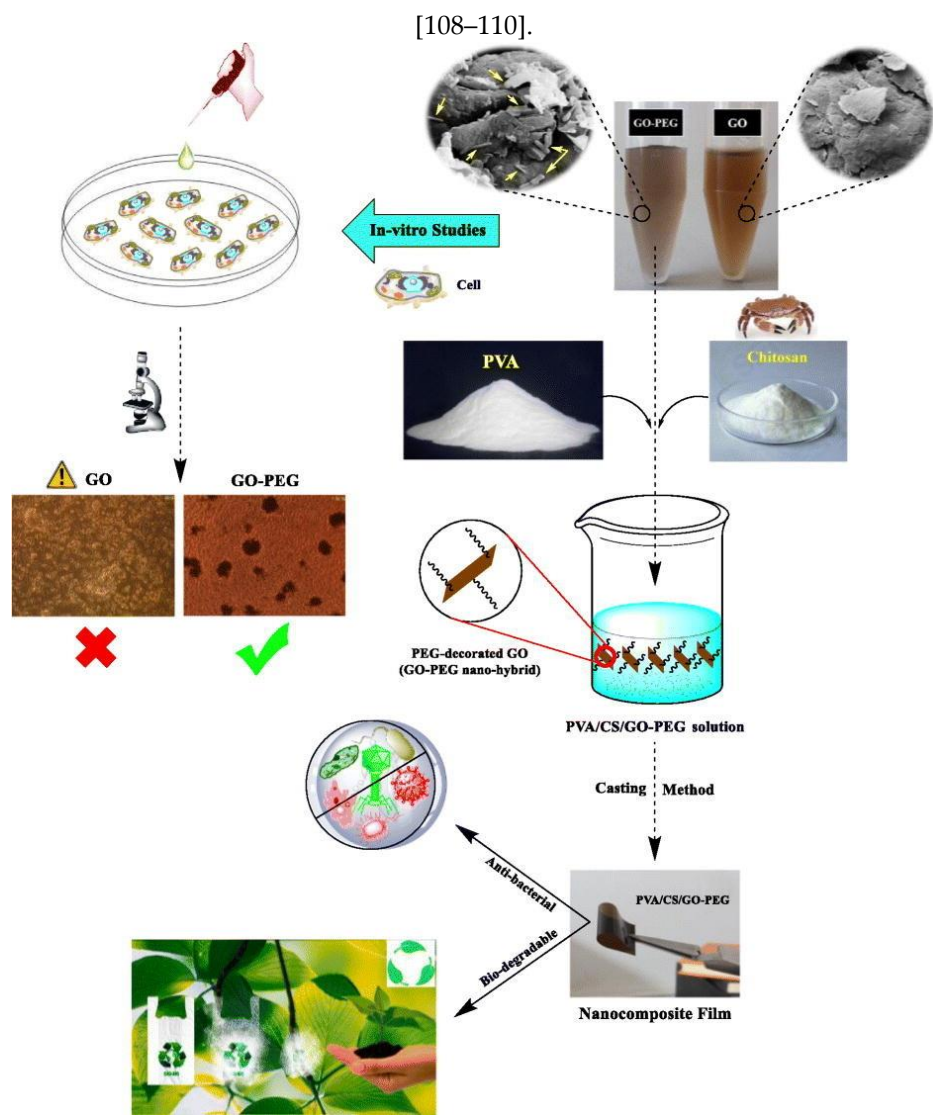


Figure 3. Synthesis strategy of biodegradable PVA/CS/GO-PEG films [103].

As listed in Table 4, several bio-derived plastic materials demonstrate potential to replace traditional synthetic polymers as next-generation pharmaceutical packaging materials. Despite their immense potential, most bio-based materials have yet to achieve large-scale production for pharmaceutical applications. As packaging materials directly contact drugs, their safety critically impacts drug quality. Rigorous experimental analysis is required to comprehensively evaluate material-drug compatibility and potential effects on pharmaceutical stability under varied storage conditions [111].

Table 4. Characteristics of different biodegradable plastics.

Bio-derived plastics	Characteristics
Polylactic acid based biodegradable plastics [112]	Good mechanical and physical properties, but poor impact resistance and high brittleness.
Starch based biodegradable plastics [113]	Good mechanical strength, strong flexibility, impact resistance, and strong temperature resistance.
Cellulose based biodegradable plastics [114]	Wide source, low cost, non-toxic and pollution-free.
Protein based biodegradable plastics [115]	Widely sourced, environmentally friendly, biocompatible, easily biodegradable, etc.

Bioactive plastic "shrelk" [116]	More sturdy and can also be used as fertilizer.
----------------------------------	---

5. Summary and Outlook

In conclusion, the physical and chemical properties of pharmaceutical packaging materials, as well as their risks of microbial contamination during production processes, are critically linked to drug quality and safety. It is imperative to strengthen research and regulation on these materials. Common materials, such as glass, plastic, metal and rubber, each of them have advantages and drawbacks: glass materials offer excellent chemical stability but may release ions; plastics are widely used but poses risks like plasticizer migration; metals provide high strength and is typically reserved for specific drug packaging; rubbers are essential for sealing but may leach additives that compromise drug quality.

Recent advancements in pharmaceutical sciences, materials science, and electronic information technology, coupled with rapid innovation in drug development, have created new demands for packaging materials. Beyond meeting basic safety and protection requirements, packaging materials must now address higher-level needs such as intelligence and sustainability: nanomaterials enhance barrier properties and mechanical strength; smart packaging enables real-time quality monitoring; eco-friendly green packaging materials reduce environmental impact while ensuring safety, and innovations in production processes further drive industry growth. These advancements will accelerate the development of pharmaceutical packaging materials, align with the evolving needs of the healthcare sector, and ultimately safeguard patient safety. With the global warming situation becoming increasingly severe, we predict that new low-carbon, environmentally friendly, and energy-efficient packaging materials and related technologies will be increasingly applied in the design, production, usage, and recycling processes of pharmaceutical packaging at an accelerated pace.

Author Contributions: Conceptualization, Y. L. and N.L.; methodology, Y. L. and N.L.; formal analysis and investigation, Y. L. N.L, C. C. and Z.C.; data collection, Y. L. N.L, C. C. and Z.C.; writing—original draft preparation, Y. L. and N.L.; writing—review and editing, Y. L. N.L, C. C. Z.C. and J. L. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by Science and Technology Project of Zhejiang Province (No.2022C01182) and Zhejiang Provincial Natural Science Foundation of China (No. LY19B010003).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Acknowledgments: We thank for its contribution of the public service platform for testing and evaluation of pharmaceutical excipients and packaging materials and industrialization of innovative achievements, ministry of industry and information technology of P. R. China.

Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

Table A1. Pharmaceutical packaging material standard system table in USP NF - 2023.

Number	Name of Standard
< 87 >	Biological Reactivity Tests, In Vitro
< 88 >	Biological Reactivity Tests, In Vivo
< 381 >	Elastomeric Closures For Injections

< 659 >	Packaging And Storage Requirements
< 660 >	Containers—Glass
< 661 >	Plastic Packaging Systems And Their Materials Of Construction
< 661.1 >	Plastic Materials Of Construction
< 661.2 >	Plastic Packaging Systems For Pharmaceutical Use
< 661.3 >	Pharmaceutical Components And Systems Used In The Manufacturing
< 665 >	Polymeric Components Used In The Manufacturing Of Pharmaceutical And
	Biopharmaceutical Drug Products
< 670 >	Auxiliary Packaging Components
< 671 >	Containers—Performance Testing
< 1031 >	The Biocompatibility Of Materials Used In Drug Containers, Medical Devices,
	And Implants
< 1136 >	Packaging Repackaging-Single-Unitcontainers
< 1177 >	Good Repackaging Practices
< 1178 >	Good Packaging Practices
< 1207 >	Package Integrity Evaluation-Sterile Products
< 1207.1 >	Package Integrity Testing In The Product Life Cycle- Test Method Selection
>	And Validation
< 1207.2 >	Package Integrity Leak Test Technologies
>	
< 1207.3 >	Package Seal Quality Test Technologies
>	
< 1660 >	Evaluation Of The Inner Surface Durability Of Glass Containers
< 1661 >	Evaluation Of Plastic Packaging Systems And Their Materials Of Construction
	With Respect To Their User Safety Impact
< 1663 >	Assessment Of Extractables Associated With Pharmaceutical
	Packaging/Delivery Systems
< 1664 >	Assessment Of Drug Product Leachables Associated With Pharmaceutical
	Packaging/Delivery Systems
< 1665 >	Plastic Components And Systems Used To Manufacture Pharmaceutical Drug
	Products

Table A2. Pharmaceutical packaging material standard system table in EP 11.0.

Number	Name of Standard
3.1	Materials Used For The Manufacture of Containers
3.1.3	Polyolefines
3.1.4	Polyethylenes Without Additives For Containers For Parenteral Preparations
	And For Ophthalmic Preparations
3.1.5	Polyethylenes With Additives For Containers For Parenteral Preparations And
	For Ophthalmic Preparations
3.1.6	Polypropylene For Containers And Closures For Parenteral Preparations And
	Ophthalmic Preparations

3.1.7	Polyethylene-Vinyl Acetate For Containers And Tubing For Total Parenteral Nutrition Preparations
3.1.8	Silicone Oil Used As A Lubricant
3.1.9	Silicone Elastomer For Closures And Tubing
3.1.10	Materials Based On Non-Plasticised Poly (Vinyl Chloride) For Containers For Non- Injectable, Aqueous Solutions
3.1.11	Materials Based On Non-Plasticised Poly (Vinyl Chloride) For Containers For Dry Dosage Forms For Oral Administration
3.1.13	Plastic Additives
3.1.14	Materials Based On Plasticised Poly (Vinyl Chloride) For Containers For Aqueous Solutions For Intravenous Infusion
3.1.15	Polyethylene Terephthalate For Containers For Preparations Not For Parenteral Use
3.2	Containers
3.2.1	Glass Containers For Pharmaceutical Use
3.2.2	Plastic Containers And Closures For Pharmaceutical Use
3.2.2.1	Plastic Containers For Aqueous Solutions For Infusion
3.2.9	Rubber Closures For Containers For Aqueous Parenteral Preparations, For Powders And For Freeze-Dried Powders

Table A3. Pharmaceutical packaging material standard system table in JP 18.

Number	Name of Standard
7	Test methods for container packaging materials
7.01	Test methods for glass containers for injection
7.02	Test methods for plastic containers for pharmaceutical products
7.03	Test methods for rubber plugs for infusion

References

1. Jaffer, G. Keys to Successful Storage Management and Transport of Biological Materials. Pharm. Salmanac 2023.

2. Nguyen, V.-T.; Linh, T.T.T.; Vo, T.-K.; Nguyen, Q.H.; Van, T.-K. Analytical Techniques for Determination of Heavy Metal Migration from Different Types of Locally Made Plastic Food Packaging Materials Using ICP-MS. Food Sci. Nutr. 2023, 11, 4030–4037.

3. Liu, X.; Zhang, Q.; Wei, Y.; Qiao, Y.; Duan, X.; Li, L.; Chen, Y.; Qian, Z. Vitrification of Cerium(III) Fluoride in Iron Phosphoborate Glasses: A Study on Redox, Structure, and Stability. Ceram. Int. 2024, 50, 38435–38444.

4. Olawore, O.; Ogunmola, M.; Desai, S. Engineered Nanomaterial Coatings for Food Packaging: Design, Manufacturing, Regulatory, and Sustainability Implications. Micromachines 2024, 15, 245.

5. Kim, O.T. Patient Safety as a Global Health Priority. Cardiovasc. Ther. Prev. 2022, 21, 3427.

6. Cheng, H.; Xu, H.; McClements, D.J.; Chen, L.; Jiao, A.; Tian, Y.; Miao, M.; Jin, Z. Recent Advances in Intelligent Food Packaging Materials: Principles, Preparation and Applications. Food Chem. 2022, 375, 131738.

7. Gomes, K.L.G.; da Silva, R.E.; da Silva Junior, J.B.; Bosio, C.G.P.; Novaes, M.R.C.G. Post-Marketing Authorisation Safety and Efficacy Surveillance of Advanced Therapy Medicinal Products in Brazil, the European Union, the United States and Japan. Cytotherapy 2023, 25, 1113–1123.

8. Gil-Pérez, I.; Rebollar, R.; Lidón, I.; Martín, J.; van Trijp, H.C.M.; Piqueras-Fiszman, B. Hot or Not? Conveying Sensory Information on Food Packaging Through the Spiciness-Shape Correspondence. *Food Qual. Prefer.* 2019, 71, 197–208.
9. Pattnaik, R.; Panda, S.K.; Biswas, S.; De, S.; Satahrada, S.; Kumar, S. Prospects and Challenges of Nanomaterials in Sustainable Food Preservation and Packaging: A Review. *Discov. Nano* 2024, 19, 178.
10. Song, T.; Qian, S.; Lan, T.; Wu, Y.; Liu, J.; Zhang, H. Recent Advances in Bio-Based Smart Active Packaging Materials. *Foods* 2022, 11, 2228.
11. Sustainability Team. Back to Sustainable Value Creation. How Sustainable Is Packaging? *Sustain. Team Discuss. Pap.* 2009, 2–3.
12. Yang, R.; Liu, H.; Ding, Z.; Zheng, J.; Mauro, J.C.; Kim, S.H.; Zheng, Q. Chemical Durability of Borosilicate Pharmaceutical Glasses: Mixed Alkaline Earth Effect with Varying [MgO]/[CaO] Ratio. *J. Am. Ceram. Soc.* 2021, 104, 3973–3981.
13. Mathaes, R.; Streubel, A. Parenteral Container Closure Systems. In *Challenges in Protein Product Development*; Warne, N., Mahler, H.C., Eds.; AAPS Adv. Pharm. Sci. Ser.; Springer: Cham, Switzerland, 2018; pp. 191–202.
14. Tian, Y.L. *Pharmaceutical Glass*; Chemical Industry Press: Beijing, China, 2015; pp. 8–10.
15. YBB00142002-2015. Guidelines for Compatibility Testing of Pharmaceutical Packaging Materials and Drugs; National Medical Products Administration: Beijing, China, 2015; pp. 446–448.
16. de Oliveira, D.P.; Costa, J.S.R.; Oliveira-Nascimento, L. Sustainability of Blisters for Medicines in Tablet Form. *Sustain. Chem. Pharm.* 2021, 21, 100423.
17. Müller, S.; Weygand, S.M. Finite Element Simulation of Stretch Forming of Aluminium-Polymer Laminate Foils Used for Pharmaceutical Packaging. *MATEC Web Conf.* 2016, 80, 16001.
18. Lebreton, L.; Andrady, A. Future Scenarios of Global Plastic Waste Generation and Disposal. *Palgrave Commun.* 2019, 5, 1–11.
19. Rahman, M.H.; Bhoi, P.R. An Overview of Non-Biodegradable Bioplastics. *J. Clean. Prod.* 2021, 294, 126218.
20. Sid, S.; Mor, R.S.; Kishore, A.; Sharanagat, V.S. Bio-Sourced Polymers as Alternatives to Conventional Food Packaging Materials: A Review. *Trends Food Sci. Technol.* 2021, 115, 87–104.
21. Yu, D.; Basumatary, I.B.; Liu, Y.; Zhang, X.; Kumar, S.; Ye, F.; Dutta, J. Chitosan-Photocatalyst Nanocomposite on Polyethylene Films as Antimicrobial Coating for Food Packaging. *Prog. Org. Coat.* 2024, 186, 108069.
22. Falk, Y.Z.; Runnsjö, A.; Pettigrew, A.; Scherer, D.; Engblom, J.; Kocherbitov, V. Interactions of Perfluorohexyloctane with Polyethylene and Polypropylene Pharmaceutical Packaging Materials. *J. Pharm. Sci.* 2020, 109, 2180–2188.
23. Jeong, Y.; Ansari, J.R.; Sadeghi, K.; Seo, J. Applicability of Polypropylene/Polyethylene Glycol/Molecular Sieve Composites as Desiccant Pharmaceutical Packaging Materials. *Food Packag. Shelf Life* 2024, 42, 101266.
24. Hazer, B.; Ashby, R.D. Synthesis of Polyvinyl Chloride/Chlorinated Polypropylene-Active Natural Substance Derivatives for Potential Packaging Materials Application. Tannic Acid, Menthol and Lipoic Acid. *Food Chem.* 2023, 403, 134475.
25. Moustafa, H.; Morsy, M.; Ateia, M.A.; Abdel-Haleem, F.M. Ultrafast Response Humidity Sensors Based on Polyvinyl Chloride/Graphene Oxide Nanocomposites for Intelligent Food Packaging. *Sens. Actuators A Phys.* 2021, 331, 112918.
26. Veronica, N.; Heng, P.W.S.; Liew, C.V. Relative Humidity Cycling: Implications on the Stability of Moisture-Sensitive Drugs in Solid Pharmaceutical Products. *Mol. Pharm.* 2023, 20, 1072–1085.
27. Amarji, B.; Kulkarni, A.; Deb, P.K.; Maheshwari, R.; Tekade, R.K. Package Development of Pharmaceutical Products: Aspects of Packaging Materials Used for Pharmaceutical Products. In *Dosage Form Design Parameters*; Tekade, R.K., Ed.; Elsevier: London, UK, 2018; pp. 521–552.
28. Nakayama, T.; Osako, M. Plastic Trade-Off: Impact of Export and Import of Waste Plastic on Plastic Dynamics in Asian Region. *Ecol. Model.* 2024, 489, 110624.

29. Meng, W.J.; Qiu, Y.X.; Yu, P.F.; et al. Research Progress on Regulations Related to Pharmaceutical Packaging Materials in China and Analytical Methods for Compatibility of Halogenated Butyl Rubber Stoppers with Drugs. *Chin. J. Pharm. Anal.* 2021, 41, 1860–1867.
30. Jia, F.F.; Zhao, X.; Yang, H.Y.; et al. Research Progress on Common Vulcanization Systems and Compatibility of Halogenated Butyl Rubber Stoppers for Pharmaceutical Use. *Chin. Pharm. Aff.* 2022, 36, 913–920.
31. Sharma, R.K.; Mohanty, S.; Gupta, V. Advances in Butyl Rubber Synthesis via Cationic Polymerization: An Overview. *Polym. Int.* 2021, 70, 1165–1175.
32. McDonald, M.F.; Shaffer, T.D.; Tsou, A.H. *Kirk-Othmer Encyclopedia of Chemical Technology*; John Wiley & Sons: Hoboken, NJ, USA, 2016.
33. Aoshima, S.; Kanaoka, S. A Renaissance in Living Cationic Polymerization. *Chem. Rev.* 2009, 109, 5245–5287.
34. Kostjuk, S.V.; Ganachaud, F. Cationic Polymerization of Vinyl Ethers: A Critical Reappraisal. *Acc. Chem. Res.* 2010, 43, 357–367.
35. Kostjuk, S.V. Recent Progress in the Cationic Polymerization of (Meth)Allyl Monomers and Macromolecular Engineering. *RSC Adv.* 2015, 5, 13125–13144.
36. Feng, J.; Cai, X.Y.; Liu, Y. Determination of Antioxidant-BHT and Vulcanizing Agent-Extractable Sulphur in Medicinal Butyl Rubber. *Chin. J. Pharm. Anal.* 2017, 37, 702–706.
37. Li, C.H.; Xue, W.L.; Xing, S.; et al. Determination of Leaching and Migration Amounts of 11 Antioxidants and Free Sulfur in Brominated Butyl Rubber Stoppers by HPLC. *Chin. J. Anal. Lab.* 2020, 39, 91–96.
38. Feng, J.; Cai, X.Y.; Liu, Y. Determination of Antioxidant-BHT and Vulcanizing Agent-Extractable Sulphur in Medicinal Butyl Rubber Stoppers. *Chin. J. Pharm. Anal.* 2017, 37, 702–706.
39. Li, Y.; Liang, T.T.; Sun, H.M. HPLC Determination of Antioxidant 1010 and Vulcanizing Agent Migration from Halogenated Butyl Rubber Stoppers for Freeze-Dried Injections into Drug Solutions. *Chin. Pharm. Aff.* 2019, 33, 283–289.
40. Li, Y.; Yang, H.Y.; Wang, F.; et al. Study on the Detection of Extractable Sulfur in Halogenated Butyl Rubber Stoppers for Pharmaceutical Use. *Chin. Pharm. Aff.* 2014, 28, 1257–1260.
41. Zhu, B.J.; Li, T.T.; Sun, H.M.; et al. Simultaneous Determination of Five Antioxidants and Free Sulfur in Halogenated Butyl Rubber Stoppers for Pharmaceutical Use by HPLC. *China Pharm.* 2018, 29, 2475–2479.
42. Mathaes, R.; Streubel, A. Parenteral Container Closure Systems. In *Challenges in Protein Product Development*; Warne, N., Mahler, H.C., Eds.; AAPS Adv. Pharm. Sci. Ser.; Springer: Cham, Switzerland, 2018; pp. 191–202.
43. Hopkins, G.H. Elastomeric Closures for Pharmaceutical Packaging. *J. Pharm. Sci.* 1965, 54, 138–143.
44. Rech, J.; Fradkin, A.; Krueger, A.; Kraft, C.; Paskiet, D. Evaluation of Particle Techniques for the Characterization of Subvisible Particles from Elastomeric Closure Components. *J. Pharm. Sci.* 2020, 109, 1725–1735.
45. Ye, Y.B.; Xu, H.; Xie, X.Y.; Fang, M. Research Progress on Compatibility of Chemical Drug Injections with Pharmaceutical Glass. *Guangzhou Chem. Ind.* 2016, 44, 50–52.
46. Almeter, P.J.; Isaacs, J.T.; Hunter, A.N.; et al. FDA Approaches in Monitoring Drug Quality, Forces Impacting the Drug Quality, and Recent Alternative Strategies to Assess Quality in the US Drug Supply. *J. Pharm. Innov.* 2022, 17, 269–282.
47. Seidling, H.M.; Woltersdorf, R. Improving Drug Therapy Safety with and for the Patient. *Bundesgesundheitsblatt* 2018, 61, 1082–1087.
48. Yang, Y.P. Silanization Treatment of Glass Containers for Pharmaceutical Packaging. Master's Thesis, Hangzhou Normal University, Hangzhou, China, 2023.
49. Bucci, M.; Deane, C.; Miura, G.; Song, Y. Research Highlights. *Nat. Chem. Biol.* 2019, 15, 651.
50. Dewhirst, R.A.; Fry, S.C. The Oxidation of Dehydroascorbic Acid and 2,3-Diketogulonate by Distinct Reactive Oxygen Species. *Biochem. J.* 2018, 475, 3451–3470.
51. Eichie, F.E.; et al. Structure and Barrier Property of Acrylate-Methacrylate Film Coating in Aspirin Microcapsules. *J. Appl. Polym. Sci.* 2006, 99, 725–727.

52. Mostafa, I.M.; Mohamed, A.A.; Alahmadi, Y.; Shehata, A.M.; Almikhlaifi, M.A.; Omar, M.A. Facile, Eco-Friendly and Sensitive Fluorimetric Approach for Detection of Chlorpromazine: Application in Biological Fluids and Tablet Formulations as Well as Greenness Evaluation of the Analytical Method. *Luminescence* 2024, 39, e4897.
53. Khalid, S.; Bilal, M.; Rasool, N.; Imran, M. Photochemical Reactions as Synthetic Tool for Pharmaceutical Industries. *Chin. Chem. Lett.* 2024, 35, 109498.
54. Bochet, C.G. On the Sustainability of Photochemical Reactions. *Chimia* 2019, 73, 720–723.
55. Egawa, G.; Kabashima, K. Barrier Dysfunction in the Skin Allergy. *Allergol. Int.* 2018, 67, 1–11.
56. Garcia-Cortes, M.; Robles-Diaz, M.; Stephens, C.; Ortega-Alonso, A.; Lucena, M.I.; Andrade, R.J. Drug Induced Liver Injury: An Update. *Arch. Toxicol.* 2020, 94, 3381–3407.
57. Antón, N.; González-Fernández, Á.; Villarino, A. Reliability and Mechanical Properties of Materials Recycled from Multilayer Flexible Packages. *Materials* 2020, 13, 3992.
58. Vrabčić-Brodnjak, U.; Yavorov, N.; Lasheva, V.; Todorova, D. Chitosan-Coated Packaging Papers—Strength and Thermal Stability. *Coatings* 2023, 13, 828.
59. Gajewski, T.; Grabski, J.K.; Cornaggia, A.; Garbowski, T. On the Use of Artificial Intelligence in Predicting the Compressive Strength of Various Cardboard Packaging. *Packag. Technol. Sci.* 2024, 37, 97–105.
60. Rahmadiawan, D.; Abral, H.; Railis, R.M.; Iby, I.C.; Mahardika, M.; Handayani, D.; Natrana, K.D.; Juliadmi, D.; Akbar, F. The Enhanced Moisture Absorption and Tensile Strength of PVA/Uncaria gambir Extract by Boric Acid as a Highly Moisture-Resistant, Anti-UV, and Strong Film for Food Packaging Applications. *J. Compos. Sci.* 2022, 6, 337.
61. Maurya, D.K.; Upadhyay, C.S.; Kumari, P. A Green Light-Weight Material for Packaging and Impact Resistant Structures. *Ind. Crops Prod.* 2024, 216, 118711.
62. Katyal, G.; Pathak, A.; Raghavendra Rao, N.G.; Grover, P.; Sharma, V.; Malik, A.; et al. Ecofriendly Pharmaceutical Packaging Material: A Review. *Mater. Today Proc.* 2024, 103, 423–431.
63. Matos, A.M.; Bonin, E.; Carvalho, V.M.; Duarte, V.; Tagiariolli, M.A.; Costa e Silva, L.F.; et al. Effect of Film Packaging or Vacuum Packaging on Characteristics Before and After Maturation of Beef from Feedlot-Finished Cattle. *PUBVET* 2020, 14, 1–11.
64. Li, H.; Pei, Q.-X.; Sha, Z.-D.; Branicio, P.S. Intrinsic and Extrinsic Effects on the Fracture Toughness of Ductile Metallic Glasses. *Mech. Mater.* 2021, 162, 104066.
65. Shukla, S.; Halli, P.; Khalid, M.K.; Lundström, M. Waste Pharmaceutical Blister Packages as a Source of Secondary Aluminum. *JOM* 2022, 74, 612–621.
66. Ciavarella, M.; Papangelo, A.; McMeeking, R. Crack Propagation at the Interface Between Viscoelastic and Elastic Materials. *Eng. Fract. Mech.* 2021, 257, 108009.
67. Mohammed, Y.H.; Namjoshi, S.N.; Telaprolu, K.C.; Jung, N.; Shewan, H.M.; Stokes, J.R.; et al. Impact of Different Packaging Configurations on a Topical Cream Product. *Pharm. Res.* 2024, 41, 2043–2056.
68. Gupta, R.K.; Pipliya, S.; Karunanithi, S.; Eswaran U, G.M.; Kumar, S.; Mandliya, S.; et al. Migration of Chemical Compounds from Packaging Materials into Packaged Foods: Interaction, Mechanism, Assessment, and Regulations. *Foods* 2024, 13, 3125.
69. Galmán Graíño, S.; Sendón, R.; López Hernández, J.; Rodríguez-Bernaldo de Quirós, A. GC-MS Screening Analysis for the Identification of Potential Migrants in Plastic and Paper-Based Candy Wrappers. *Polymers* 2018, 10, 802.
70. Kwansa, A.L.; Pani, R.C.; DeLoach, J.A.; Tieppo, A.; Moskala, E.J.; Perri, S.T.; Yingling, Y.G. Molecular Mechanism of Plasticizer Exudation from Polyvinyl Chloride. *Macromolecules* 2023, 56, 4775–4786.
71. Wen, Y.-H.; Lee, C.-F.; Chen, Y.-J.; Chang, G.-J.; Chong, K.-Y. Risks in Induction of Platelet Aggregation and Enhanced Blood Clot Formation in Platelet Lysate Therapy: A Pilot Study. *J. Clin. Med.* 2022, 11, 3972.
72. Jiang, C. Evaluation of the Compatibility between Pharmaceutical Packaging Materials and Drugs Based on National Standards of Pharmaceutical Packaging Materials. *Eng. Manag.* 2025, 6, 267–269.
73. Bai, F.; Chen, G.; Hu, Y.; Liu, Y.; Yang, R.; Liu, J.; Cai, H. Understanding the Effect of Plastic Food Packaging Materials on Food Flavor: A Critical Review. *Trends Food Sci. Technol.* 2024, 148, 104502.
74. Wei, B.; Zhao, Y.; Xu, M.S. Research Progress on the Relationship between Protein Structure Changes and in vitro Digestibility under Different Treatment Methods. *Food Sci.* 2019, 40, 327–333.

75. Chen, S.; Quan, D.H.; Sam, G.; Ozberk, V.; Wang, X.T.; Halfmann, P.; Rehm, B.H.A. Assembly of Immunogenic Protein Particles toward Advanced Synthetic Vaccines. *Small* 2023, 19, 2205819.
76. Zhang, F.; Li, D.; Wang, C.; Liu, Z.; Yang, M.; Cui, Z.; Chen, X. Shape Morphing of Plastic Films. *Nat. Commun.* 2022, 13, 7294.
77. Gupta, D.; Bhatt, S.; Shukla, P.; Kumar, A. Microbial Contamination in Pharmaceutical Manufacturing. *J. Drug Discov. Health Sci.* 2024, 1, 21-27.
78. Saeed, M.; Ilyas, N.; Arshad, M.; Sheeraz, M.; Ahmed, I.; Bhattacharya, A. Development of a Plant Microbiome Bioremediation System for Crude Oil Contamination. *J. Environ. Chem. Eng.* 2021, 9, 105401.
79. Wada, S.; Satoh, Y.; Hama, T. Massive Loss and Microbial Decomposition in Reproductive Biomass of *Zostera marina*. *Estuar. Coast. Shelf Sci.* 2022, 275, 107986.
80. Luoreng, Z.-M.; Wang, X.-P.; Mei, C.-G.; Zan, L.-S. Comparison of microRNA Profiles between Bovine Mammary Glands Infected with *Staphylococcus aureus* and *Escherichia coli*. *Int. J. Biol. Sci.* 2018, 14, 87-99.
81. WHO. Guidelines on Packaging for Pharmaceutical Products. WHO Tech. Rep. Ser. 2002, 902, Annex 9.
82. Holbein, M.E. Understanding FDA Regulatory Requirements for Investigational New Drug Applications for Sponsor-Investigators. *J. Investig. Med.* 2009, 57, 688-694.
83. Herber, O.R.; Gies, V.; Schwappach, D.; Thürmann, P.; Wilm, S. Patient Information Leaflets: Informing or Frightening? A Focus Group Study Exploring Patients' Emotional Reactions and Subsequent Behavior towards Package Leaflets of Commonly Prescribed Medications in Family Practices. *BMC Fam. Pract.* 2014, 15, 163.
84. White, N.D.; Kibalama, W. Prevention of Pediatric Pharmaceutical Poisonings. *Am. J. Lifestyle Med.* 2018, 12, 117-119.
85. Jafarzadeh, S.; Nooshkam, M.; Zargar, M. Green Synthesis of Nanomaterials for Smart Biopolymer Packaging: Challenges and Outlooks. *J. Nanostruct. Chem.* 2023, 13, 1-24.
86. Rukmanikrishnan, B.; Ismail, F.R.M.; Manoharan, R.K.; Kim, S.S.; Lee, J. Blends of Gellan Gum/Xanthan Gum/Zinc Oxide Based Nanocomposites for Packaging Application: Rheological and Anti-Microbial Properties. *Int. J. Biol. Macromol.* 2020, 148, 1182-1189.
87. Patil, A.S.; Waghmare, R.D.; Pawar, S.P. Photophysical Insights of Highly Transparent, Flexible and Re-emissive PVA@WTR-CDs Composite Thin Films: A Next Generation Food Packaging Material for UV Blocking Applications. *J. Photochem. Photobiol. A* 2020, 400, 112647.
88. Razali, M.H.; Ismail, N.A.; Amin, K.A.M. Titanium Dioxide Nanotubes Incorporated Gellan Gum Bio-nanocomposite Film for Wound Healing: Effect of TiO₂ Nanotubes Concentration. *Int. J. Biol. Macromol.* 2020, 153, 1117-1135.
89. Tang, H.; Xiong, H.; Tang, S.; Zou, P. A Starch-Based Biodegradable Film Modified by Nano Silicon Dioxide. *J. Appl. Polym. Sci.* 2009, 113, 34-40.
90. Ramakanth, D.; Singh, S.; Maji, P.K. Advanced Packaging for Distribution and Storage of COVID-19 Vaccines: A Review. *Environ. Chem. Lett.* 2021, 19, 3597-3608.
91. Sharma, D.K.; Gupta, P.; Priety. Internet of Things: The New Rx for Pharmaceutical Manufacturing and Supply Chains. In *An Industrial IoT Approach for Pharmaceutical Industry Growth*; Academic Press: London, UK, 2020; pp. 257-288.
92. Saha, E.; Rathore, P.; Parida, R.; Rana, N.P. The Interplay of Emerging Technologies in Pharmaceutical Supply Chain Performance: An Empirical Investigation for the Rise of Pharma 4.0. *Technol. Forecast. Soc. Change* 2022, 181, 121799.
93. Yang, G.; Xie, L.; Mäntysalo, M.; Zhou, X.; Pang, Z.; Xu, L.D.; Kao-Walter, S.; Chen, Q.; Zheng, L.-R. A Health-IoT Platform Based on the Integration of Intelligent Packaging, Unobtrusive Bio-Sensor, and Intelligent Medicine Box. *IEEE Transactions on Industrial Informatics* 2014, 10, 2180-2191.
94. Botcha, K.M.; Chakravarthy, V.V.; Anurag. Enhancing Traceability in Pharmaceutical Supply Chain Using Internet of Things (IoT) and Blockchain. *Proc. IEEE Int. Conf. Intell. Syst. Green Technol. (ICISGT)* 2019, 445-453.
95. Kumarka, A.; Guptanv, B.; Lalasap, C. A Review on Packaging Materials with Anti-Counterfeit, Tamper-Evident Features for Pharmaceuticals. *Int. J. Drug Dev. Res.* 2013, 5, 26-34.

96. Leem J. W.; Jeon H.; Ji Y.; Park S. M.; Kwak Y.; Park J.; Kim K.; Kim S.; Kim Y. L.; Edible Matrix Code with Photogenic Silk Proteins. *ACS Cent. Sci.* 2022, 8, 5, 513–526.
97. Lotoshynska, N.; Izonin, I.; Nazarkevych, M. Consumer-Centered Design of the Secondary Packaging for Industrial Pharmaceuticals. *CIRP J. Manuf. Sci. Technol.* 2021, 32, 257–265.
98. Wang, S.; Yu, P.; Fan, G. Application Research of Smart Pharmaceutical Packaging Materials in the Multisensory Dimension. *Packag. Eng.* 2022, 43, 76–87.
99. Zadbukén, N.; Shahi, S.; Gulecha, B. Recent Trends and Future of Pharmaceutical Packaging Technology. *J. Pharm. Bioallied Sci.* 2013, 5, 98–110.
100. Zhou, D.; Xiong, L. Intelligent Design of Pharmaceutical Packaging under the Background of Healthy China Initiative. *Packag. Eng.* 2022, 43, 235–239.
101. Udayakumar, G.P.; Muthusamy, S.; Selvaganesh, B. Biopolymers and Composites: Properties, Characterization and Their Applications in Food, Medical and Pharmaceutical Industries. *J. Environ. Chem. Eng.* 2021, 9, 105322.
102. Lin, H.; Tian, S.; Mei, L. Research Progress of Pharmaceutical Packaging Materials. *Chin. J. Pharm.* 2023, 54, 339–346.
103. Mohammadi, S.; Babaei, A. Poly(vinyl alcohol)/Chitosan/Polyethylene Glycol-Assembled Graphene Oxide Bionanocomposites as a Prosperous Candidate for Biomedical Applications and Drug/Food Packaging Industry. *Int. J. Biol. Macromol.* 2022, 201, 528–538.
104. Khalil, H.P.S.A.; Davoudpour, Y.; Saurabh, C.K. A Review on Nanocellulosic Fibres as New Material for Sustainable Packaging: Process and Applications. *Renew. Sustain. Energy Rev.* 2016, 64, 823–836.
105. Yuan, C.; Hou, H. Application and Prospect of Bioplastics in Food and Pharmaceutical Packaging. *Chin. J. Pharm.* 2020, 51, 1356–1363.
106. Ren, Y.; Ren, J. Polylactic Acid Pharmaceutical Packaging Material, Its Preparation Method and Application. CN Patent 101914273A, 2010.
107. Dejene, B.K.; Gudayu, A.D. Eco-Friendly Packaging Innovations: Integrating Natural Fibers and ZnO Nanofillers in Polylactic Acid (PLA) Based Green Composites - A Review. *Polym.-Plast. Technol. Mater.* 2024, 63, 1645–1681.
108. Zhu, X. Discussion on the Optimal Application of Pharmaceutical Packaging Materials and the Development Trend of New Materials. *China Packag.* 2022, 42, 30–34.
109. Thyavihalli Girijappa, Y.G.; Mavinkere Rangappa, S.; Parameswaranpillai, J.; Siengchin, S. Natural Fibers as Sustainable and Renewable Resource for Development of Eco-Friendly Composites: A Comprehensive Review. *Front. Mater.* 2019, 6, 226.
110. Sanjay, M.R.; Arpitha, G.R.; Naik, L.L. Natural Fibers as Sustainable and Renewable Resource for Development of Eco-Friendly Composites: A Comprehensive Review. *Nat. Resour. J.* 2016, 7, 108–114.
111. Faruk, O.; Bledzki, A.K.; Fink, H.P.; Sain, M. Biocomposites Reinforced with Natural Fibers: 2000–2010. *Prog. Polym. Sci.* 2014, 39, 9–26.
112. Xie, B.; Bai, R.R.; Sun, H.S. Research Progress on the Synthesis, Biodegradation and Waste Disposal of Polylactic Acid Plastics. *Chin. J. Biotechnol.* 2023, 39, 1912–1929.
113. Cheng, Y.Z.; Ding, X.; Wu, Y. Research Progress on the Preparation of Bioplastics from Crop Wastes. *Eng. Plast. Appl.* 2022, 50, 172–176.
114. Zhang, Z.C.; Sun, Z.Y.; Wang, X. Research Progress and Prospect of Cellulose-Based Biodegradable Plastics. *Eng. Plast. Appl.* 2022, 50, 168–172.
115. Zhang, J.X.; Wang, Y.Z.; Chen, H. Research Progress of Bio-Based Plastics Based on Animal and Plant Proteins. *Leather Sci. Eng.* 2021, 31, 9–15.
116. Lei, Y.J. Reading the "Script" of Plastic Reduction from the Source of Production and Use. *Environ. Econ.* 2021, 19, 18–23.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.