

SPECIAL SUSTAINABLE BIOMEDICAL MATERIALS APPLICATION AND MEDICAL WASTE REUSE AND RECYCLING- A REVIEW

Abstract

This study examines manufacturing techniques for medical and dental synthesis and characterization. Several medical settings have benefited from thinking about biological materials and devices. Additional benefits from MONP features and evidence of nanometal oxide's applicability in nanomedicine research were summarized in this paper. There has been a lot of focus on the dangers of MONPs to the body and the antibacterial properties of green-generated nano-oxides. Lignin is a versatile biomass with several uses due to its antioxidant, biocompatibility, antibacterial, and anti-UV properties. Natural Lignin can be processed in several different chemical ways; after these processes, the refined Lignin can be turned into functionalized Lignin, which can be employed in developing high-quality biomaterials. Therefore, Lignin is a prospective biomaterial for various applications, such as drug and gene delivery, biosensors, bioimaging, 3D printing, and tissue engineering. The benefits of reusing and recycling medical waste are highlighted, along with the processes, components, and chemical makeup of each methodology used in modern waste management. As plastics are the most commonly used material in healthcare, we also examine chemical and mechanical recycling methods for plastics and potential approaches to, and challenges with, reusing or recycling biomedical items.

Keywords: bioengineering, medical engineering, biomedical materials, Recycling, Medical waste.

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I. INTRODUCTION

Rapid progress in bioengineering, which includes medical, dental, and tissue engineering, regenerative medicine, and cell therapies, is mainly responsible for the current high standard of biomedical materials. Medical diagnostics and intricate interventional procedures necessitate highly advanced machinery. The term "biomaterial" refers to materials with desirable medical and dental equipment characteristics, for example, being able to interact with the body's living tissues without causing any harm[1].

With the use of nanotechnology and interdisciplinary study, novel nanosized materials with desirable physical and chemical properties have been developed for use in biomedicine. One typical use of nanotechnology is the fabrication and manipulation of matter on the nanoscale scale, which allows for realizing previously impossible size-dependent properties [3]. The optimal size for nanoparticles (NPs) used in nanomedicine is less than 200 nm. The bioavailability of nanoparticles (NPs) is enhanced because of their small size and high surface area [3,4]. They are able to enter the lungs, circulate in the blood, and bind to endothelial cells. Due to their many useful properties, such as high stability, ease of preparation, ability to be engineered to the desired size, shape, and porosity, absence of swelling variations, adaptability to both hydrophobic and hydrophilic systems, and surface negativity, which facilitates functionalization by a wide range of molecules, metal oxide NPs (MONPs) are becoming increasingly popular as a biomedical tool[5].

In today's world, numerous processes and tools are needed for biomaterials' production and synthesis. Typically, they are techniques for sourcing the required raw materials for fabricating a custom prosthesis or implant using state-of-the-art material processing technology. Diagnostic materials and sustained medication release systems both necessitate advanced technological development. The manufacturing cycle for biomaterials is becoming increasingly dependent on technologies developed during the current phase of the industrial revolution [6].

About 15%-35% of lignocellulosic biomass is Lignin, which is the second most abundant natural substance after water [7]. Lignin is obtained from the wood and paper processing sectors. It is essential in producing plant cell walls [8] and comprises cross-linked polyphenolic compounds that give plants structural strength. Commercial usage of industrial lignin waste now amounts to less than 2% [9,10]. In 2019, the worldwide lignin market was valued at USD 954.5 million, and it is expected to expand by 2% per year until 2027 [11]. Large-scale manufacturing's requirement for Lignin and a growing appreciation for environmental sustainability have reignited the hunt for its valuable functions. The biomedical industry extensively uses natural polymers in applications as varied as medication delivery and tissue engineering [12], including chitin, chitosan, alginate, and cellulose. Since the 1970s, lignocellulosic biomass, mainly cellulose, as a biomedical material because of its high strength, ease of production, biodegradability, and safety. Over the years, numerous cellulose variants have been created and proven to benefit the market [13]. Examples include nanocrystalline cellulose, bacterial cellulose, nano wood, and micro/nanofibril cellulose.

The term "healthcare waste" describes the byproducts of medical facilities such as hospitals, clinics, and laboratories. There are two main categories of medical trash: non-hazardous rubbish (which accounts for around 85% of healthcare waste and is analogous to

domestic waste) and hazardous garbage (which may contain biological, chemical, radioactive, and physical characteristics). When medical waste is not handled appropriately, it can pose concerns to healthcare workers and the public [14]. Infectious or drug-resistant germs spread, dangerous chemicals and pharmaceutical waste are improperly disposed of, and harmful air pollutants are released as primary causes [14,16]. Treatment options for medical waste are depicted in (Fig. 1), including the most common thermal treatment and chemical, radiation, biological, and mechanical approaches. Both incineration and autoclaving are examples of thermal treatment commonly used to dispose of hazardous material. Dioxins, furans, and heavy metals are unwanted byproducts of incineration [15]. In addition, 2,2,2-trifluoroethanol and other organic solvents used in the pharmaceutical industry might lead to incinerator corrosion. [14,16].



Figure 1: Current Medical Waste Treatment Strategies [16].

1. Biomaterials Application in Medicine and Dentistry: Dependence on biomaterials in the medical industry. The term "biomaterial" refers to any material other than a drug or treatment that is utilized to supplement or replace the tissues of an organ or part of an organ[17]. Biomaterials have the necessary biotolerance (biocompatibility), which means they are biologically compatible and interact with living stuff harmoniously. The term "biotolerance" refers to a state of equilibrium between living organisms and their environment. The optimally biotolerant biomaterial does not elicit any sort of tissue reaction, either short- or long-term, or inflammation. It does not prevent the surrounding severed tissue from developing normally. As a general rule, biotolerance is defined as the inability to develop toxicological or immunological reactions to a substance or to recover from tissue irritation [18]. Implants can be roughly categorized as shown in (Figure 2). Some simple criteria can be used to classify these materials. Therefore, this figure uses a variety of graphic representations to highlight various criteria. Essential needs for implants and other biomaterials are outlined in (Table 1) [1,18,19].

Table 1. Materials specifications for use in surgical implants [1]

Mechanical Properties	Technological Properties	Biotolerance
<ul style="list-style-type: none"> • tensile strength, • yield point, • fatigue strength, • hardness, • abrasion resistance, • stiffness, • plasticity (elongation, contraction), • ductility (resistance to fracture). 	<ul style="list-style-type: none"> • ensuring the assumed quality of the biomaterial, • ensuring the required quality of the surface and the implant, • suitability of the material and product for effective sterilization, • minimal manufacturing costs. 	<ul style="list-style-type: none"> • reactions with tissues and body fluids, • stability of ownership: • mechanical, • physical, • chemical, • degradation related to: • local damage to the implant (harmful changes), • systematic corrosion effects (harmful damage).

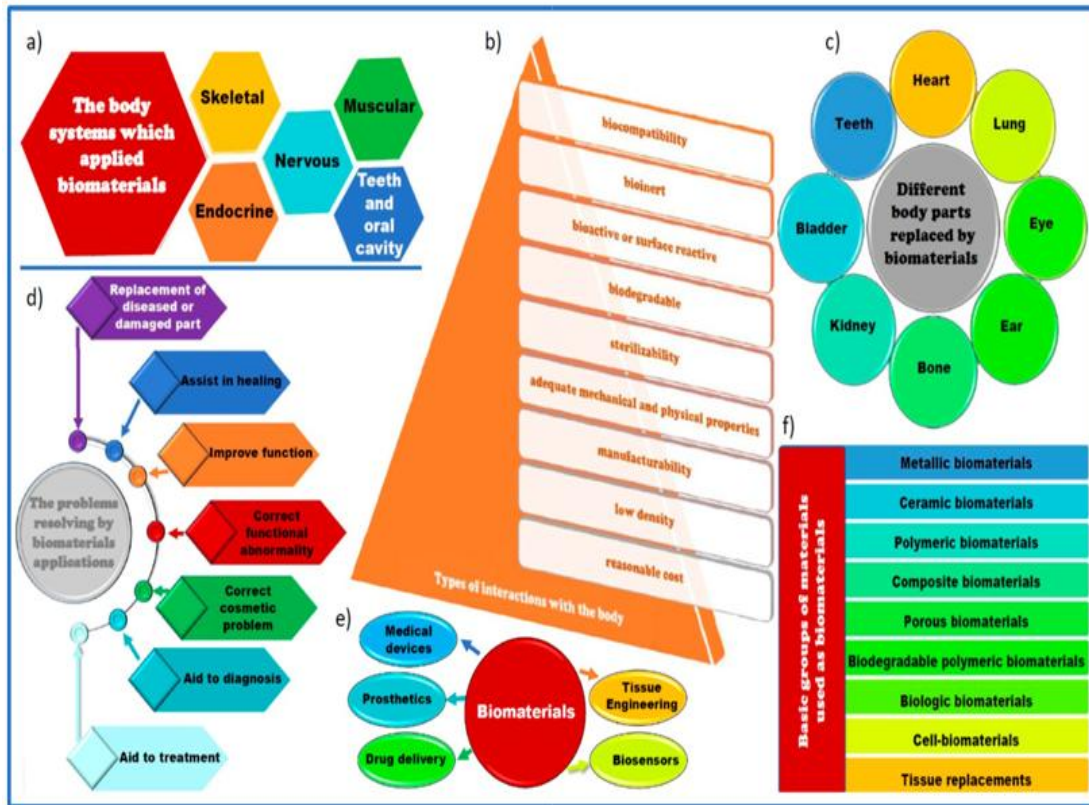


Figure 2: Biomedical Materials are Broadly Categorized According to the Following Criteria: (A) The Body Systems Which Applied Biomaterials; (B) Types the Interactions With The Body; (C) Different Body Parts Replaced by Biomaterials; (D) The Problems Resolving By Biomaterials Application; (E) Applications Areas of Biomaterials; (F) Primary Groups of Materials Used Asbiomaterials [1].

Biological systems, including cells, tissues, proteins, and organs, frequently come into contact with biomedical materials. Classification of medical equipment is based on the following criteria: The first is the actual touching or interacting with the body, the second is touching injured skin, the third is touching internal organs (like the heart or the circulatory system), the fourth is the invasiveness of the holes in the body, and the fifth is the implantation itself. Sixth, providing the body with energy or nutrients; seventh, year duration [19].

Under the definition of engineering material and often built from biomedical materials, a comprehensive classification of medical devices is provided in (Table 2). Collagen injections for removing soft tissue abnormalities are an example of a chemical employed alone. Although they do not strictly speak to the concept of engineering materials, they are often grouped with the appropriate biological materials. Biomaterials have increased use in bioengineering, regenerative medicine, and tissue engineering due to technological advancements [1,19].

Table 2. Classification Scheme for Medical Equipment [1].

The Main Criterion for Classification	Medical Device Groups	Medical Devices Subgroups	Comment
period of use of medical devices	transient (<60 min)		
	short-term (<30 days)		
	long-term (>30 days)		
degree of invasiveness	invasive devices (penetrating deep into the body through an opening in the body or its surface)	surgical	as a result of a surgical procedure, they are introduced inside the body or under its surface
		implanted	intended to be completely introduced into the body or to replace the epithelial surface or the surface of the eye as a result of a surgical intervention
	active devices	surgical instruments	
		medical	their operation depends on the conversion of feed energy other than directly generated by the body or gravity
		therapeutic	
	Implants	diagnostic	
		surgical	placed in the intended place in the body by surgical methods
		other	for example, needles, drains, filters
		implanted prostheses	internal prostheses or endoprostheses that physically replace an organ or tissue
	a field of medical use or a specific location in the body	Implants	artificial organs
orthopedic			used to support, replace or supplement temporarily or permanently bone, cartilage, ligaments, tendons or associated tissues
oral			used to improve, enlarge, or replace any hard or soft tissue in the mouth involving the maxilla, mandible, or temporomandibular joint
craniofacial			used to correct or replace hard or soft tissues in the craniofacial area except for the brain, eyes and inner ear
dental			used to replace missing teeth

2. Nano-Oxides: Biofluids and cell biomolecules, once NPs have been ingested, play a role in the particle's physical transport into the interior cellular structures. Controlled synthesis approaches aim to produce NPs with specific morphological configurations, sizes, distributions, and stabilities, as these parameters influence the biological response to NPs [20].

- **Shape and Size:** Biodistribution and material absorption can be affected by size since it impacts the surface-to-volume ratio. Due to their ability to propose sufficient circulation time and compatibility with the mammalian vasculature's pore size (5 nm), NPs in the intermediate size range (20-100 nm) have the most significant potential for in vivo application. Hydrodynamic size plays a significant role in how NPs are distributed and eliminated from the body [21].
- **Surface Area and Surface Energy:** Size and shape heterogeneity of NPs arise from their loss of thermodynamic stability as their surface area and energy grow. The electro-neutrality between anions and cations is broken when the periodicity of the crystal is disturbed, forcing oxygen atoms with a lower coordination number to the

surface of crystal oxide NPs[22]. Numerous edges and corners on the particles provide opportunities for reactive surface sites. As a result of their high surface-to-volume ratio and the plethora of active sites it affords, NPs' reactivity may be controlled despite their diminutive size and unusual shape. More often than larger particles, those with a larger surface area come into contact with the cell[23].

- **Crystal Structure:** When NPs interact with cells, they frequently produce metal ions, which can have hazardous effects [24]. Dissolution is affected by various factors, including crystallinity, crystal phase, surface strain, size, defects, and media composition. Due to the high free energy, surface ions are more likely to separate from NPs due to their proximity to the corners and edges [25,26].
 - **Dispersibility and Aggregation:** The high concentration of MONPs (1000 ppm) causes them to clump together, probably because of van-der-Waals forces, elevated surface energy, and magnetic attraction. How well nano oxides assemble affects their biodistribution, biology, and medicine [27].
 - **Surface Properties:** Since positively charged NPs are attracted electrostatically to the negatively charged cell membrane, they are regarded to be more harmful than neutral NPs. Compared to negatively charged NPs, positively charged NPs showed a greater ability for opsonization (adsorption of plasma proteins), suggesting that their interaction with antibodies, serum proteins, etc., may alter the structure of the adsorbed molecules and their activity [28].
 - **Photocatalytic Activity:** The most widely accepted process for photocatalysis involves the localization of electrons in tiny hydrogen-rich locations and the generation of holes trapped in surface imperfections. Increased photocatalytic, electrochemical activity, and antibacterial impact result from the charge separation, reducing the likelihood of hole-electron recombination [29]. When water molecules in air or a solution are oxidized, they trap the positive holes and release -OH radicals, which are highly reactive oxygen species (ROS). When conduction band electrons reduce oxygen, superoxide radicals are formed, which then react with hydrogen ions to form peroxide radicals (-OOH) or hydrogen peroxide (H₂O₂) [30].
- 3. Applications of MONPs in Biomedicine:** MONPs can only be used in a certain context if they meet certain requirements. For instance, MONPs employed as pharmaceutical carriers need to degrade naturally and have a kinetics that satisfies the requirements of treating a particular infection without resorting to intrusive surgery. TiO₂, ZnO, CuO, ferric oxide (Fe₂O₃), and ferrous oxide (Fe₃O₄) appeared to be relatively safe for mammals; however, there is a wide variety of MONPs available [31].
- **Internal Tissue Therapy:** To influence growth factor expression, cell division, cell differentiation, migration, apoptosis, and other cellular processes, therapies must be able to affect a complex molecular signaling system [32]. Breathing in MONPs, swallowing them, injecting them intravenously, applying them topically, or transporting them to a specific organ through nanofibers are all viable entry routes. The ability of nanomedicine to construct nanocarriers with increased delivery

efficiency due to translocation through the cell membrane is a significant benefit to the field of disease prevention and cure [33]. Improving pharmacological activity, prolonged and focused administration of many therapeutic agents, stability, and bioavailability are just a few advantages of creating nanocarriers as drug-delivery vehicles. The toxicity of a nanoparticle does not follow a regular pattern once it has entered the target cell. (Figure 3) provides an overview of the interactions occurring in the circulatory system and the shared pathways through which MONPs generate cytotoxicity [34].

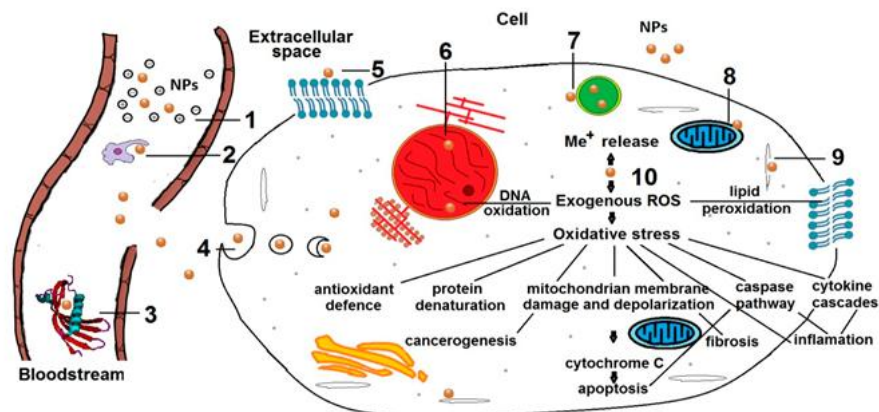


Figure3. Mechanisms of Metal Oxide Nanoparticles (Monps) Delivery Pathway and Cell Damage in Eukaryotic Cells: (1) Interaction With Ions in Circulation; (2) Ingestion by Phagocytic Cells; (3) Opsonization Or Enzymic Degradation; (4) Internalization Via Endocytosis After Extravasation to the Extracellular Space Or (5) Membrane Perforating And Damage of its Components and their Function; (6) Chromosomal Aberrations and Changes in Cell Replication Rate; (7) Lysosome Rupture; (8) Mitochondria Damage; (9) Lower Growth Rate, Structural Changes and Shorten Lifetimes of Microtubules if the Cytoskeleton; (10) Generation of ROS, Oxidative Stress and Subsequent Processes [34].

NPs' ability to target specific areas allows for a lower total dose of the medication, resulting in fewer negative side effects. The toxicity of NPs and their unwanted interactions must be reduced while their selectivity for cancer and other target cells increases. Nanocarriers for transport and targeting are coupled to natural polymers like polysaccharides and polyesters as well as synthetic polymer materials that are then conjugated with inorganic NPs like silica, MOs, HAP, and so on (Fig. 4) [34].

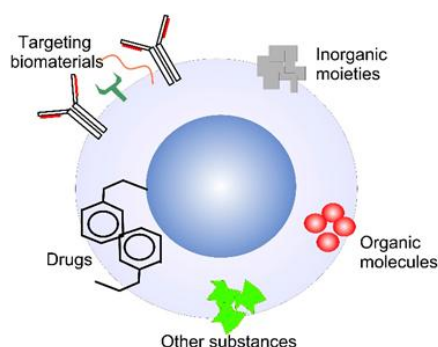


Figure4: Scheme of Possible Modifications of Monps for Biomedical Applications [34].

- **Iron Oxide Nanoparticles:** The magnetic properties of iron oxide nanoparticles (NPs) make them useful for a number of diagnostic and therapeutic applications, such as the magnetic separation of biological products and cells [35]. The goal of treatment with magnetic biomaterials like Fe₃O₄ NPs is to have them removed from the body once they have served their purpose. Osmosis in the bloodstream enables the detection and elimination of iron oxide nanoparticles [37].
- **Zinc Oxide Nanoparticles:** ZnO NPs are employed in cancer therapy due to their superior ion release in acidic environments and higher ROS generation, making them preferentially lethal toward cancer cells in vitro and in vivo[38].
- **Titanium Dioxide Nanoparticles:** Because of its beneficial effects on cell adhesion, osseointegration, cell migration, and wound healing, TiO₂ finds extensive usage in the biomedical industry, particularly in the fields of bone and tissue engineering. Tumor growth inhibition in glioma-bearing mice was observed in vivo trials with non-modified TiO₂ under 365 nm light irradiation, and an increase in mouse survival accompanied this [39].
- **Iron Oxides Nanoparticles:** The therapeutic efficacy of vaccines can be enhanced by using iron oxide nanoparticles as the carrier. Putting small interfering RNA (siRNA) on nanocarriers was the key to successfully halting viral reproduction [40].
- **Zinc Oxide Nanoparticles:** Biomarkers for immunotoxicity, such as cytokines and chemokines, have been shown to be induced by ZnO NPs. The effects of the adjuvant are mediated by a variety of pathways, including stimulation of the innate immune response, improvement of antigen uptake by antigen-presenting cells, and regulation of the cytokine network [37].
- **Immuno-Therapy:** Small particles (NPs) have the potential to modulate immune system activity through interactions with specific cells and molecules. Nanoparticles (NPs) can be engineered to both dampen (anti-inflammatory) and heighten (vaccine) immune responses. The immune system recognizes NPs as foreign substances after blood proteins have absorbed them; the type and amount of these proteins determine the NPs' fate through interacting with other molecules[34,41].
- **Iron Oxides Nanoparticles:** The therapeutic efficacy of vaccines can be enhanced by using iron oxide nanoparticles as the carrier. Integrating small interfering RNA (siRNA) onto nanocarriers was one method utilized to suppress viral replication [40] successfully.
- **Zinc Oxide Nanoparticles:** Immunotoxicity can be measured with biomarkers like cytokines and chemokines, and it has been shown that ZnO NPs can stimulate their production. There were a variety of adjuvant effects noted, including as stimulation of antigen-presenting cells better to absorb antigens and control the cytokine network[37].

- **Diagnosis:** MONPs' fluorescent or magnetic properties have made them widely used in diagnostics. Nano-oxides have advantages that make it possible to see and measure disease with greater accuracy and clarity [34].
- **Quantum Dots for Labeling:** In the field of biomedicine, highly fluorescent NPs could be utilized to label a wide range of targets, from cancer cells and stem cells to microorganisms and even single molecules. Sized between 2 and 10 nm, quantum dots (QD) are colloidal semiconductor NPs that are both highly fluorescent and photostable [42]. In vivo imaging of cellular structures and processes can benefit significantly from such a device. This allows for tracking cell migration, viability testing, and target site retention. QDs produce light with a high quantum yield and a crisp, symmetrical emission spectrum when excited. Their primary features are a controlled electron/ion transfer effect, photo- and chemical stability, and catalytic capabilities. However, It is crucial that these QDs be used safely once they have been introduced into the organism. Therefore, we looked into the intramuscular and intracardiac delivery of iron oxide nanoparticles as a labeling agent for in vitro studies of a human skeleton myoblast cell line [43].
- **Contrast Agents for Magnetic Resonance Imaging:** Due to its high spatial resolution, 3D anatomical information, absence of ionizing radiation, and good soft-tissue contrast, magnetic resonance imaging (MRI) has become a routine non-invasive clinical treatment. Diseases like cancer can be diagnosed, and their prognoses accurately predicted using magnetic imaging technology, which allows for counting various molecular alterations associated with the onset and development of pathological states [44].
- **Nano-Oxides in Dentistry:** The primary objective of endodontic treatment is to eradicate bacterial infection in the root canal system so that microorganisms do not hinder periapical healing[34].
- **Nano-Oxides in Hard Tissue Regeneration:** The bioactivity of the conventional titanium-based materials used in orthopedic and dental implants is inadequate with respect to osseointegration with bone [34].
- **Nano-Oxides for Wound Healing:** MONPs are used in hard tissue restoration and polymeric nanofibers to enhance the overall properties of the composite scaffold used in skin tissue engineering [34].
- **Nano-Oxides Used as Biosensors:** For a nanobiosensor to work, it must first detect the presence of a ligand and then bind to a receptor. Some publications [46] have categorized nanobiosensors into piezoelectric, electrochemical, semiconductor, optical, and calorimetric categories based on their detecting mechanism (signal measurement). These methods convert the data into electrical signals. Electrode material plays a critical role in the development of high-performance electrochemical sensing platforms for detecting target molecules using various advanced analytical methods [34,47].

- **Antimicrobial Nano-Oxides:** Toxic effects caused by NPs' interactions with bacteria are often used in antimicrobial applications in sectors such as the food and agriculture industries [34].
- **Titanium Dioxide Nanoparticles:** The anatase phase of TiO₂ is the most effective ROS producer, according to the results [48].
- **Zinc Oxide Nanoparticles:** In order to be effective as an antibacterial agent and as UV light protection in cosmetics, ZnO NPs need to have strong optical absorption in the UVA and UVB spectrum.
- **Copper Oxide Nanoparticles:** CuO NPs are far less expensive than AgO NPs, but they need to be used in higher concentrations to have the same antibacterial effect.
- **Silver Oxide Nanoparticles:** A benefit of silver is that it is poisonous against bacteria even when used in very small doses [49]. It is commonly agreed that bacteria cells can be lysed or killed by exposure to high concentrations of lyre-active silver ions.
- **Magnesium Oxide Nanoparticles:** In addition to their employment as heat agents in cancer therapy, MgO NPs also serve as a trigger for the post-activation of the bone-repair scaffold [50].
- **Calcium Oxide Nanoparticles:** The generation of reactive oxygen species (ROS) in the presence of CaO NPs benefited from the higher pH, just as it did in the presence of MgO NPs, which aided in antibacterial activity. Contact between NPs and bacteria is crucial for the bactericidal activity of both MgO and CaO[51].
- **Aluminum Oxide Nanoparticles:** Alumina NPs were found to be effective against *E. coli*, but only at very high concentrations [52]. Al₂O₃ NPs generated using the co-precipitation approach showed substantial antibacterial action against *E. coli*, as well as *P. vulgaris*, *S. aureus*, and *S. mutans* [53]. These NPs were irregular in shape and measured in the range of 35 nm in size.
- **Iron Oxide Nanoparticles:** Both magnetite (Fe₃O₄) and maghemite (Fe₂O₃) point to materials with a single crystalline structure that are both biocompatible and superparamagnetic. Magnetic attraction between NPs and high-energy surfaces causes them to cluster. In order to achieve the recycling of nanosized silver, combining Fe₂O₃ NPs with Ag NPs could prevent coalescence and environmental contamination [54].
- **Nickel Oxide Nanoparticles:** Depending on the bacterial species and concentration, NiO NPs were found to have either bactericidal or bacteriostatic activity. We synthesized Nickel-based Gadolinia doped ceria with spherical shape and size between 40–70 nm with composition NiO-Ce_{0.8}Gd_{0.2}O_{2-δ} via co-precipitation [55].

- **Cerium Dioxide Nanoparticles:** CeO₂ has a strong antioxidant potential [56] because, unlike other NPs, it reduces the rate of ROS generation generated by H₂O₂. This effect is dose-dependent. CeO₂ NPs exhibited antibacterial action against both gram-positive and gram-negative bacteria, with the most striking results seen against the latter [57]
4. **lignin:** Lignin is biosynthesized from three hydroxycinnamyl alcohols or monolignols: *p*-coumaryl, coniferyl, and sinapyl. An enzyme-mediated dehydrogenative polymerization converts *p*-coumaryl, coniferyl, and sinapyl into *p*-hydroxyphenyl (H), guaiacyl (G), and syringyl (S) respectively. (Fig. 5) illustrates the conversion of monolignols into their corresponding polymer units [59].

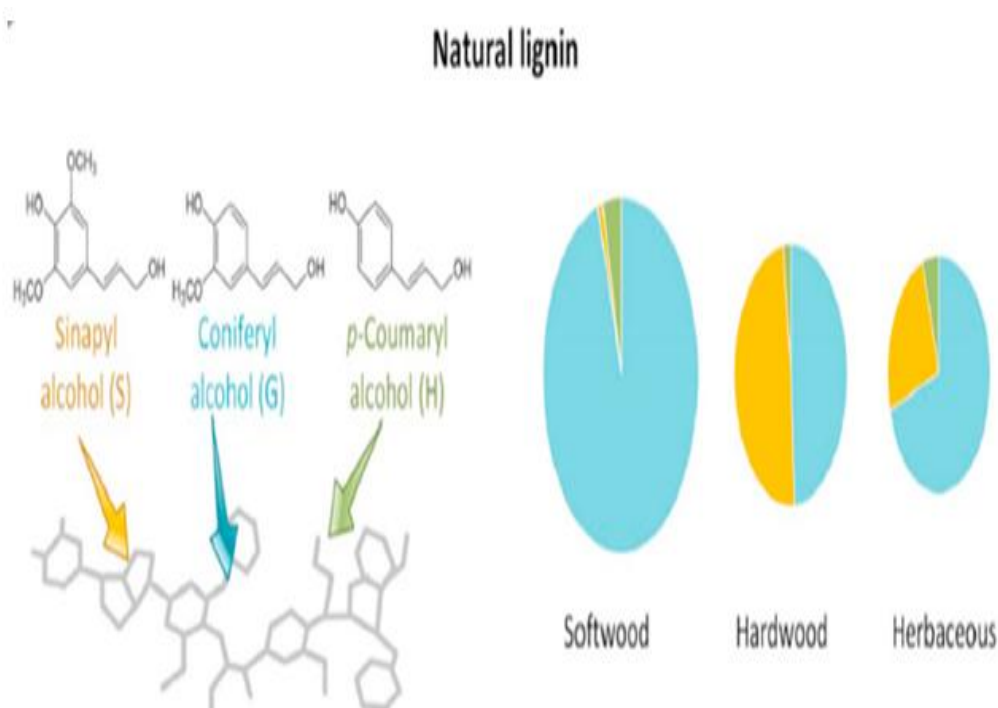


Figure 5: Compositions of Natural Lignin in Different Types of Plants [59].

In contrast to other assessments, this one delves further into Lignin's existing and future uses in biomaterials. Lignin's antioxidant, antibacterial, anti-UV, and biocompatibility properties, as well as cutting-edge techniques for modifying the molecule, were described, along with its myriad potential medical applications. Tumor therapy, bioimaging/biosensors, tissue engineering, and 3D printing are only few of the possible medical uses of lignin that are depicted in (Figure 6).

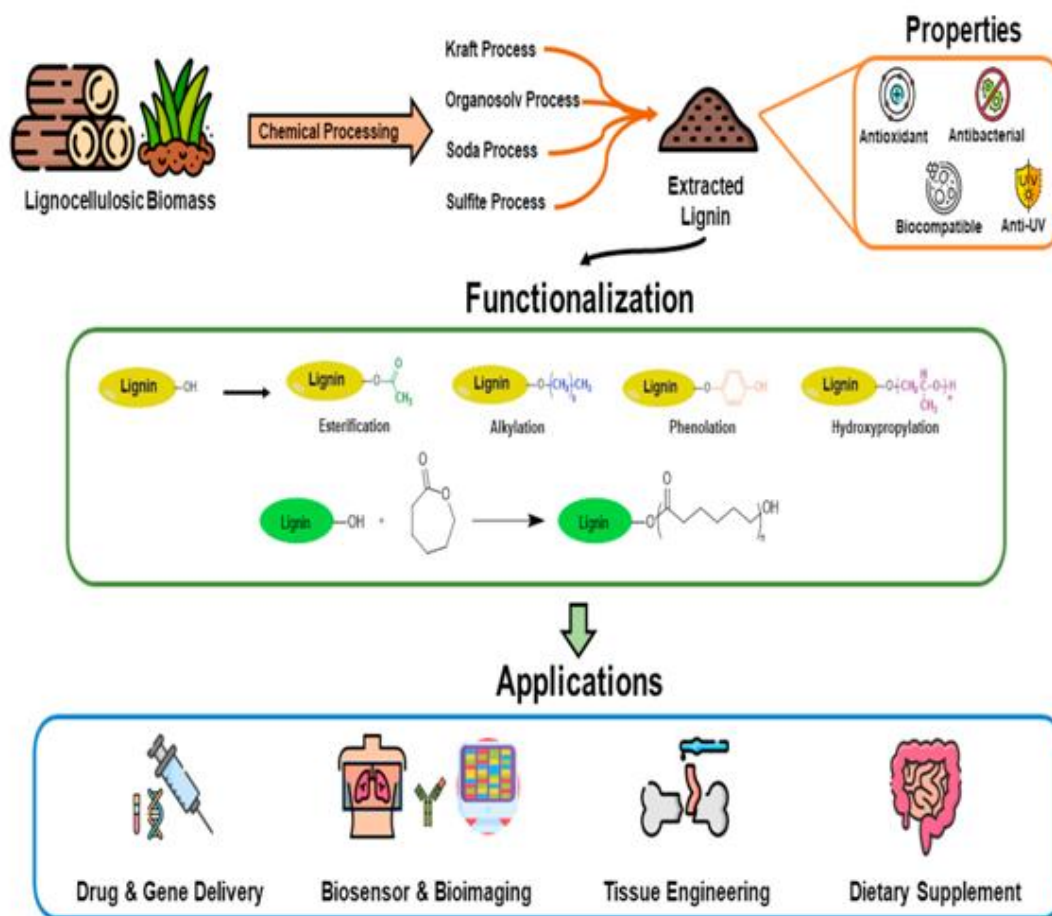


Figure 6: Overview of Lignin as a Biomaterial [59].

5. Types of lignins: Lignin can come in various forms, depending on how it's processed. This group includes kraft, organosolv, soda lignins, and lignosulphonates. About 85 percent of the world's lignin supply is kraft lignin. For the production of kraft lignin, wood chips are dissolved in white liquor, a solution of sodium hydroxide and sodium sulfide with an initial pH between 13 and 14 [63]. The many forms of Lignin are summarized in (Table 3).

Table 3: Summary of different lignin types.

Type of Lignin	Source of Lignin	Solubility	Mw (Da)	Characteristics	Applications
Kraft lignin	Softwood, Hardwood	Alkali, organic solvents	3700–19,800	Lower content, phenolic groups, high S, high OH	High levels of antioxidants, antimicrobials, and UV protection; easily adaptable for use in

					biomedicine [60]
Lignosulfonate	Softwood, Hardwood	Water	12,000 – 60,000	High S content, water-soluble, high MW and PDI, self-association, and agglomeration in aqueous solution	Powerful against free radicals, viruses, blood clots, ulcers, and cancer, High sulfur concentration makes it unsuitable for biomedical usage [61].
Soda lignin	Annual plants	Alkali	1300–10,400	Sulfur-free, more p-hydroxyl units, and carboxyl groups, high silicate and Ni content	anti-inflammatory properties, Low yield makes it unlikely to be useful [62].
Organosolv lignin	Softwood, Hardwood , Annual plants	Wide range of organic solvents	4100–10,800	Sulfur-free, higher chemical purity, lower Mw, very hydrophobic	High antioxidant, antimicrobial, and anti-UV activities, and Easy to modify for biomedical applications [60].

6. Lignin Properties for Biomedical Applications

- Antioxidant:** Antioxidants are chemicals that can eliminate free radicals or stop them from forming in food and biological systems. Medications aren't the only manufactured things that include antioxidants. Butylated hydroxytoluene (BHT) is one type of synthetic antioxidant that sees widespread application [64]. Although they function well as antioxidants, they are also known to be cytotoxic and carcinogenic, even in low quantities [65]. As a result, there is a pressing need for safe, effective, naturally occurring antioxidants to replace the currently used toxic antioxidants. The high concentrations of phenolic and oxygen-containing functional groups in Lignin are commonly cited as the reason for the compound's antioxidant quality. These lignin functional groups efficiently react with free radicals in the system, ending oxidative chain reactions [59].

- **Antibacterial:** Many infectious diseases have bacteria as their root cause, although antibiotics can cure some. Since the discovery of penicillin in 1928, several traditional antibacterial drugs have been generated in the drug pipeline, and these have been vital in saving millions of lives [66]. Because of its low price and ease of availability, antibiotics have been overused, which has led to the rise of resistant strains of bacteria [67]. As a result, researchers must constantly work to create brand-new alternatives to traditional antibacterial drugs. Antimicrobial compounds are found in plants, polymers, and metals.

Despite silver nanoparticles (AgNPs) promising antimicrobial and antifungal properties [68], antiviral drugs are that natural processes do not easily break them down. Lignin is a natural biopolymer that shows promise as a building block for eco-friendly materials [69]. Its activity against bacteria is attributed to its phenolic fragment, which possesses a double bond in the $C\alpha = C\beta$ position of the side chain and a methyl group in the γ position [70]. In general, it was hypothesized that phenolic compounds' antibacterial activity was achieved through their interaction with bacteria, which resulted in membrane damage and bacterial lysis [59].

- **Anti-Ultraviolet:** Light with wavelengths between 200 and 400 nm is known as ultraviolet (UV) or the ultraviolet region of the electromagnetic spectrum. In addition to UV-A (320-400 nm) and UV-B (280-320 nm), and UV-C (200-280 nm), there is also UV-B (280-320 nm) radiation. The ability of ultraviolet light to ionize molecules and, in turn, trigger chemical processes sets it apart from the visible light spectrum [71]. UV radiation has been shown to photodegrade organic compounds or polymers, in addition to its well-established negative effects on the human body, such as destroying DNA molecules [72]. The development of UV-shielding materials, especially eco-friendly bio-based and sustainable materials, has garnered more attention. Lignin, along with melanin and cellulose, has been investigated by scientists for its potential as a UV filter [73,59].
 - **Biocompatibility/Biosafety:** Many scientists are interested in using biocompatible polymers like polysaccharides and proteins as medication and gene nanocarriers [74]. The ability of a biomaterial to coexist with a human body and elicit a suitable host response in a given context is its defining characteristic. The biocompatibility of biomaterials prepared from natural sources like plants is often high. There have not been as many studies looking at Lignin's biocompatibility as there have been for other prevalent plant-based natural polymers like cellulose and pectin [75].
- 7. Modification of Functional Groups:** Lignin can be altered without disrupting its native polymer structure. There have been many suggestions for chemical changes to Lignin to make it more reactive, less brittle, and more solvent-soluble in organic solvents. In addition, the biocompatibility of biopolymers is improved by the insertion of essential functional groups into modified lignins, which improves the blending of Lignin with other polymers in the production of new biomaterials. Adding additional chemical sites to Lignin is a standard process, as shown in (Fig. 7) [59,76].

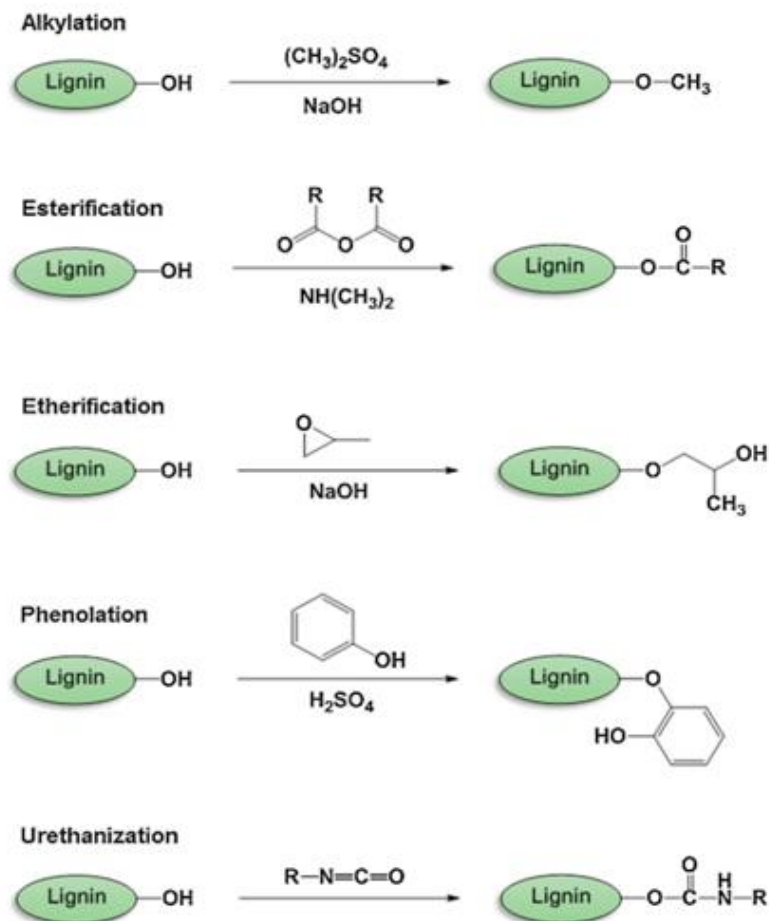


Figure 7: Overview of Chemical Modifications of Lignin [59].

8. Applications of Lignin-Based Materials

- Lignin as Drug and Gene Delivery Vehicle:** Targeted drug delivery and controlled drug release are two methods that can increase the therapeutic efficacy of drug and gene delivery systems. To securely distribute the medications to specific regions, it is necessary to discover improved natural and biocompatible materials. Searching for improved delivery vehicles, such as nanoparticles, encapsulation, and microspheres, is crucial in creating new medication and gene delivery systems. Lignin-derived biomaterials offer desired features like antimicrobial, antioxidant, and biocompatibility, making them an attractive candidate for use as a medication and gene delivery vehicle. The higher surface-to-mass ratio of engineered nanoparticles compared to other particles makes them particularly valuable in biomedicine. Nanoparticles' ability to bind, adsorb, and transport bioactive substances, including medicines, genes, and proteins, is significantly boosted by this property [77].
- Drug Encapsulation:** Since Lignin can encapsulate lipophilic medicines, this opens the door to the possibility of regulated and targeted drug release, which has

applications in cancer and tumor therapy. Lignin's potential as a biomaterial is enhanced by the many ways in which it may be modified and used, such as its self-assembly into nanoparticles and the production of grafted Lignin by ATRP and ROP [59].

- Gene Delivery:** The low cytotoxic character of Lignin has made it a promising carrier in recent gene transfer research. In the present day, poly ethylenimine (PEI) is widely utilized for gene transfection, despite the fact that it also adds to the dose-dependent cytotoxicity [78]. Lignin, with its minimal cytotoxicity, was shown to be a promising alternative to PEI for this purpose. The negatively charged DNA does not have a binding site in Lignin. Possible solutions were explored, including the utilization of lignin-based nanotubes and the functionalization of Lignin with possible DNA binding sites.
- Biosensors and Bioimaging:** The bioreceptor in a biosensor recognizes the analyte and transmits information about it in the form of a biological signal. An electrical signal is generated from this signal by a transducer. A biological analyte's concentration in a sample can be inferred from the corresponding electrical signal [79]. The transducer determines whether a biosensor is electrochemical, optical, thermal, or piezoelectric [80]. Lignin's potent compatibility with carbon-based materials and efficient adsorption onto sp^2 -hybridized carbon surfaces can be attributed to its high aromatic subunit content. Silver nanoparticles are only one type that Lignin can help keep in place. The biocompatibility of Lignin makes it an attractive candidate for use in biosensing and bioimaging [81]. Using (Fig. 8) as an illustration, one can build an electrochemical biosensor for glucose analysis [59]. See (Table 4) for a synopsis and significant discoveries about Lignin's use in biosensors and bioimaging.

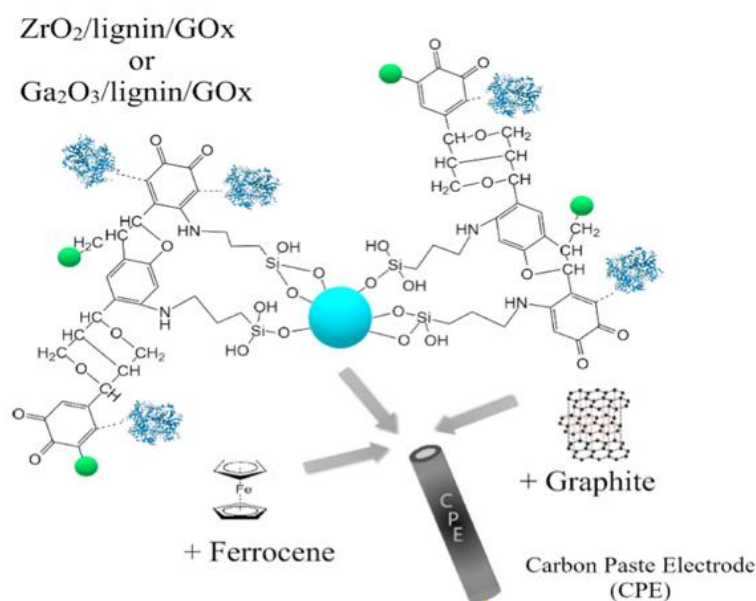


Figure 8: Biosensor Construction Based on Ga_2O_3 /lignin/GOx or ZrO_2 /lignin/GOx material [59].

Table 4: Summary and critical findings of lignin-related biosensors and bioimaging applications.

Type of Lignin	Matrix Material	Form	Key Findings
Kraft lignin	Silica Glucose oxidase	Biosensor	A two-fold increase in glucose oxidase immobilization (25.28 mg/g) Successful linear response glucose detection (0.5–9 mM) with a detection limit (145 μM) and high sensitivity (0.78 μA/mM) [82]
Kraft lignin	Magnetite Polydopamine Glucose oxidase	Biosensor	High glucose oxidase loading (29.44 ± 2.39 mg/g) Comparable glucose detection sensitivity and accuracy with commercial biosensors [83]
Kraft lignin	Gallium oxide Zirconium (IV) oxide Glucose oxidase	Biosensor	24.7 and 27.1 mg/g glucose oxidase immobilization Successful glucose detection [84]
Lignin from wood	-	Bioimaging	Good fluorescence ability and photostable for 30 days. About 10–30% of radical scavenging behavior [85]
Alkali lignin	-	Biosensor	Excellent sensitivity for hydrogen peroxide detection as low as 0.13 nM Low cytotoxicity (≥90.32% cell viability) [86]
Lignin	-	Bioimaging	Biocompatible and low cytotoxicity (≥80% cell viability) Good photoluminescence for imaging of HeLa cells [87]
Alkali lignin	Silver	Biosensor	Hydrogen peroxide detection across 10 ⁻¹ – 10 ⁻⁶ M with high sensitivity and linear relationship [88]
Organosolv lignin	Concanavalin A Horseradish peroxidase Glucose oxidase	Biosensor	Suitable for glucose detection using chromogenic substrates Better or comparable limit of detection at 0.85 μM [89]
Lignosulfonate	Nitrogen MXene/Prussian blue	Biosensor	Successful detection behavior for hydrogen peroxide (0–10 mM), glucose (10 μM–5.3 mM), lactate (0–20 mM), and alcohol (0–50 mM) across broad concentrations [90]
Corn stover lignin	Magnetite Anti-prion protein aptamer	Biosensor	10-fold sensitivity improvement and successful detection of prion protein across 0.1–200 ng/mL [91]

Organosolv lignin	Antigenic p17-1 peptide sequence	Biosensor	Successful detection of specific anti-p17 human immune deficiency virus antibodies as low as 0.1 ng/mL [92]
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- Tissue engineering:** Tissue engineering is a branch of regenerative medicine that focuses on creating biocompatible functional materials by applying multiple scientific disciplines. Tissue engineering is a cutting-edge approach to repairing, replacing, enhancing, and conserving damaged or diseased biological tissue or organs. Numerous research on the potential use of Lignin in various materials and processing methods for tissue engineering applications have been done due to the complex macromolecule's non-toxic, ultraviolet-protecting, antioxidant, and antibacterial properties [59].

9. Reprocessing and Reusing Biomedical Materials: It is typical practice in waste management to reprocess and reuse medical materials and devices to maximize economic and environmental benefits [93]. Health concerns arise from not strictly adhering to the processes and recommendations for reprocessing and sterilizing multi-use medical devices. Determining the best strategy for reprocessing and reusing a biological material depends heavily on its resistance to degradation throughout the cleaning, disinfection, and sterilizing processes. Methods of sterilizing that work well with plastics are shown in (Fig. 9). As disposable medical equipment has become more common, plastics have replaced more traditional biomedical materials like glass, metal, and ceramic. There are three types of sterilization processes: (i) heat sterilization, (ii) radiation sterilization, and (iii) chemical sterilization [94]. The thermal treatments used for heat-resistant materials are steam sterilization (autoclaving, restricted to moisture-resistant materials) and dry heat sterilization [16]. Surgical alloys and instruments are susceptible to corrosion and rust when subjected to autoclaving [94]. Blood bag polyvinyl chloride (PVC) has been shown to lose its plasticizer under repeated autoclaving while simultaneously losing molecular weight and gaining tensile modulus and yield strength [16,95].

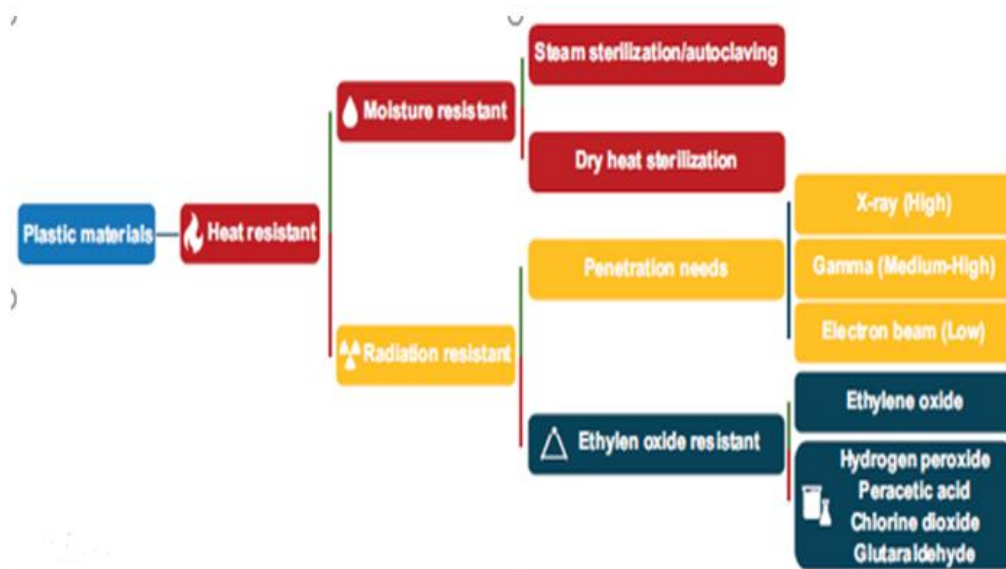


Figure 9: Decision Tree for Plastic Material Sterilization Method Selection [16].

10. Recycling and Recovery of Biomedical Materials: Product recycling involves breaking down existing items into their parts and then repurposing those parts into something else [93]. Plastics are widely used for medical devices because they outperform more expensive materials like steel, ceramic, and glass in terms of durability, cost, and flexibility. Because of this, recycling plastics is essential. However, many other types of waste are also recyclable, such as the stainless steel used in surgical instruments, medical implants, and dental prosthetics collected from the cremation industry, mercury from dental amalgams [96], and aluminum from waste pharmaceutical blister. Plastic and microplastic pollution affects at least 12 of the United Nations' Sustainable Development Goals, demonstrating the importance of recycling plastic-based items [97].

11. Mechanical Recycling of Plastic-Based Biomedical Materials: The possibility of recycling medical waste by mechanical means has been investigated in several studies. The blue wrapping paper made from polypropylene (PP) that was once used to package surgical instruments is now being utilized to injection mold brand-new pieces of medical equipment. The mechanical properties of recycled materials made from injection molding of melted wrapping paper waste were very constant across a wide range of melting temperatures, and the resulting products were resistant to degradation after up to 10 cycles of disinfection [98].

Due to the widespread distribution of personal protective equipment (PPE), such as surgical face masks, during the COVID-19 epidemic, there has been a growth in interest in recycling these products through mechanical and chemical pathways to develop new materials for application in a variety of industries (Fig. 10). Producing sound-absorbing porous materials from PP-based face masks with performance similar to commercial counterparts [99] is one example of the enormous potential of utilizing recycled face masks in construction applications. Shredded face masks (SFM) added to concrete had no impact on its compressive (about 5% increase) or tensile (roughly 3% decrease) strengths, and the material performed similarly in spalling and frost resistance tests. Incorporating 1.5% SFM into hot mix asphalt significantly increased the asphalt pavement's resistance to rutting and decreased the rutting depth by 69% [100].

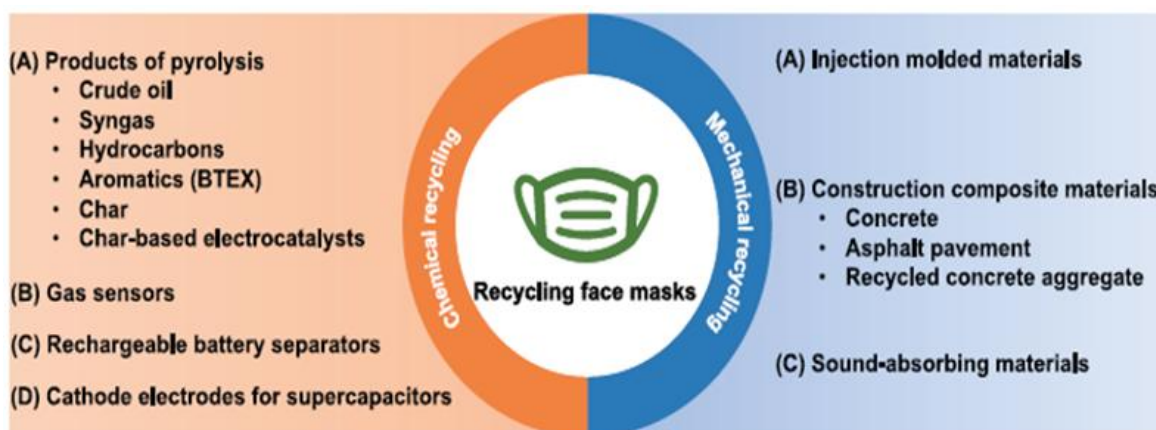


Figure10: Recycling Face Masks Via Chemical Or Mechanical Methods to Yield a Variety of Products [16].

12. Chemical Recycling of Plastic-Based Biomedicalmaterials: Damaged and heterogeneous plastics can be processed in tertiary recycling with minimal to no additional cleaning. Pyrolysis is a promising thermochemical treatment of medical waste since it does not require pre-sorting waste plastics [101]. Pollution and carbon emissions can both rise with the use of several other thermal treatments. This method has been successfully used for numerous medical waste types, resulting in marketable results. Physically, the pyrolysis oil made from recycled PP syringes was comparable to diesel fuel and gasoline blends due to alkanes, alkenes, and aromatic rings. Catalytic conversion of PP, PE, and nylon-6 disposable masks over nickel/sulfur dioxide (Ni/SO₂) catalysts in a carbon dioxide (CO₂) reaction medium produced syngas and C1-2 hydrocarbons. Long-chain hydrocarbons were converted to methane and hydrogen on the Ni/SO₂ catalyst, and carbon monoxide (CO) generation was enhanced in the CO₂ medium [16,102].

13. Challenges and Outlook in Recycling Andreusing Medical Waste: There are a few obstacles to recycling medical waste, including the lack of a uniform sorting system and the potential for spreading dangerous diseases. Because most medical wastes are not infectious, they can be recycled. However, the high expenses of treating infectious waste have arisen partly because of the incorrect disposal of objects that should not have been classified due to a lack of standardized medical waste categorization [103]. Machine learning algorithms may be the answer to this problem since they have already been used in the recycling of plastics, bottles, and municipal solid waste with an accuracy of over 90% [104]. Better biomedical waste management may result from educating healthcare staff on the topic. In addition, public awareness should be enhanced, and stringent rules should be enacted for medical waste recycling to address social and ethical problems arising from the health dangers associated with recycling infectious medical waste [105]. Healthy design approaches should be incorporated into the design of plastic-based items to ensure their recyclable nature and economically feasible solutions should be developed to facilitate plastic recycling. Bio-based plastics are another viable option with the potential to lessen negative environmental impacts and, with further study, lower recycling costs than petroleum-based competitors in the medical field [16,105].

II. CONCLUSION

MONPs have tremendous potential as antibiotic alternatives that can kill multidrug-resistant microbes. Redox-active MONPs modulate the innate and adaptive immunity of humans. This property could be exploited for purposes such as improving vaccine response or modulating immunological tolerance in the face of autoimmunity, allergies, or cancer. Although the potential for MONPs to be used as molecular imaging agents, drug carriers, and cancer treatments is high, there are still several obstacles that must be overcome before they can be implemented in clinical or industrial settings. Despite MONPs' enormous biological potential, the lack of control over ROS distribution to tissues or cells is a fundamental limitation of ROS-based therapy. However, there are still undiscovered methods of cellular and extracellular functioning of MONPs that are unconnected to ROS formation.

Although Lignin's biocompatibility has been the subject of much research, its underlying mechanisms remain obscure. More research is required to understand how Lignin affects cellular components, including proteins and DNA. Although some bacteria and fungi may naturally break down Lignin, whether or not the human body can break it down is still

debatable. Environmental and public health problems related to the dramatic increase in medical waste generation and the disadvantages of existing disposal methods may be alleviated by introducing recycling and reuse programs. Reprocessing and reusing medical devices have environmental and financial benefits over traditional disposal techniques. However, to avoid contamination, defined processes must be followed. Alternative methods that may allow for effective management of biomedical material waste include recycling and recovery. Unfortunately, recycling initiatives still face difficulties selecting, designing, and sterilizing materials. To summarize, resources should be allocated to enable sustainable waste management programs in healthcare sectors through recycling and reusing biological products.

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