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Applications of Bioremediation in Biomedical Waste Management: Current and Future Prospects

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HIGHLIGHTS

- Illustration of problems of hospital waste management
- Impact of improper biomedical waste on human health and environment.
- Discussion of usefulness of bioremediation in managing hospital waste.

Abstract: Biomedical waste management is an integral part of health care as being the mainstay of hospital cleanliness, hygiene, and maintenance activities. Medical care is crucial for human health but mismanagement of biomedical waste harms the flora and fauna of ecosystem on earth, and badly influences the human health. Due to their stability, biomedical wastes are not eliminated by the solid or sewage treatment plants, and get bioaccumulated in environment, and eventually get to population through various means. They are harmful due to their potential carcinogenicity, genotoxicity, mutagenicity, and other toxicities. Current disposal techniques employed in disposing biomedical wastes are sewage/drains, incineration, and landfills. These practices are normally costly and might transform pollutants from one toxic form to another. Whereas bioremediation is an inexpensive method of employing naturally occurring microorganisms or plants to detoxify man-made pollutants to harmless products that make soil fertile as well in the process. Researchers have also evolved genetically engineered microbes to remediate environmental pollutants including radionuclides. Phytoremediation is also a type of sustainable methods, which is reasonable and competent in handling heavy metals and radioactive waste generated from hospitals. In this article, we have summarized rational applications of bioremediation techniques of using effective microorganisms and plants in enhanced removal of several recalcitrant pollutants including biomedical waste. Our review highlights the challenges and future perspectives to bioremediate non-biodegradable and potentially toxic hospital wastes.

Keywords: Bioremediation; genomics; hospital waste; microbial remediation; phytoremediation; radioactive waste.

INTRODUCTION

Wastes are unwanted materials produced out of human activities, and that are dumped into soil, water, or air. A huge variety of biomedical wastes are produced in hospital and clinical settings during diagnosing and curing of the diseases and immunization, such as used needles, sharps, infected dressings and body organs, various diagnostic samples of blood and urine, drugs, medical devices, chemicals, and radioactive materials [1]. Also, academics and research activities add on these wastes carrying pathogens including bacteria, fungi and viruses, toxic chemicals, and radiation [2]. Therefore, biomedical wastes carry higher risk of infections and hazards compared to other waste category, and it becomes mandatory that all such waste materials should be properly collected at the site of origin and treated well to dispose of safely [1]. Generally, pre-treatments of hospital wastes demand larger storage space or specific techniques that are both ideal and lawful, to prevent influences on society and the environment [3].

Soil acts as a geochemical sink for pollutants and open dumping or burning of the toxic and infectious waste materials result in contamination of crops and underground water. Improper handling of unused or expired drugs in pharmaceutical industries, and stock raising farms are damaging the aquatic environment [4,5]. It has been found that majority of non-steroidal anti-inflammatory drugs such as diclofenac, ibuprofen, ketoprofen, and naproxen are not fully degraded, and due to their immovability, they are not entirely eradicated by the sewage treatment plants. Eventually, they could incorporate back to humans by consuming tap water [5]. Therefore, biomedical waste management is applied as an integral part of health care. It includes all the efforts and arrangements involved to manage waste from its origin to its final disposal.

Also, hospital solid waste has been reported to comprise of heavy metals such as Cd, Zn, Pb and Cu. A recent study by Selman and coauthors [6] had shown presence of high concentrations of heavy metal in the ash of incinerated waste from hospital in Iraq. Such kinds of waste material when dumped into soil, get accumulated in the environment as they are non-biodegradable [7]. Moreover, modern day hospitals are progressively using radioisotopes for diagnostic and therapeutic applications for various diseases including cancer. Therefore, substantial amount of radioactive waste is produced and discarded into the environment, and typically persist non-degraded. This poses life-threatening hazards to the personnel involved in these settings, and even to general population if they get exposed to it through mismanaged radionuclides wastes [8]. Management of wastes containing heavy metals and radionuclides are scarce and expensive, suggesting a more economic and sustainable alternative such as bioremediation. This approach uses microorganisms or plants to remediate contaminated soil or water [3,9].

Considering this, the present review focuses on recent research on the microorganisms - in the successful enhancement of remediation of emerging pollutants including pharmaceutical and microplastics As waste disposal approaches of non-incineration types are being recommended and encouraged by World Health Organization to manage biomedical waste, the progress of bioremediation as described in this review could be a breakthrough to improve the skills in managing recalcitrant hospital wastes.

NEED OF BIOMEDICAL WASTE MANAGEMENT

Exposure to nonbiodegradable and hazardous hospital wastes are indeed absolute source of transmission of life-threatening diseases like HIV/AIDS, Hepatitis B, and others [10]. The waste containing many deadly microorganisms, their toxins and particularly recent Corona Virus are posing a risk of infection relapse and occurrence of future infection waves. Workers who are involved in taking care of such a waste are at risk of getting exposed to Covid-19 and other dangerous biological agents by punctures/cuts, contaminated sharps, skin-mucous contact/projection of blood or biological fluids, ingestion, or inhalation of contaminated particles [11].

Considering the impact of biomedical waste on to the environment and human health, we need to adapt cost-effective and eco-friendly methods for its disposal [12]. Despite being an indispensable component of quality assurance in hospitals, many health care personnel are less responsive of the appropriate management of biomedical waste. Safe waste management protects hospital staff, the public, and the local environment [13].

A cross sectional survey from Njue and coauthors [14] in public health facilities in Thika Subcounty, Kenya, reported that full adherence to the seven waste disposal guidelines was low [16.3%]. Knowledge on waste segregation, waste separation then disposal and means of transports were not strictly followed and insignificantly different among nurses and waste handlers. From this finding, compliance remains a key challenge. Kwikiriza and coauthors [15] conducted a study about handling of hospital waste in Bwindi Community Hospital, Uganda. They observed that clinical staff had awareness of type and risk of waste but the knowledge of non-clinical staff handling waste disposal was much poorer, resulting in improper separation of clinical and compostable waste at source, and inaccurate onsite transportation. Chemical waste emptied to underground bodies and further tracing of disposal was not possible. A study from Khalid and coauthors [16] surveyed hospital waste management [HWM] practices in teaching hospitals of Peshawar, Pakistan. The questionnaire-based response revealed the lack of HWM practices in all surveyed hospitals. No appropriate separation of waste from generation point to final disposal was performed. In surveyed hospitals, 56.3% of hospitals were found with the incinerator facility while 43.7% practiced open dumping. Moreover, the operational parameters of the incinerators were non-satisfactory as these units were established in thickly inhabited areas and emanating hazardous gases. Therefore, biomedical waste management demands immediate academic attention and awareness in the form of various training courses as well [12,17]. However, the eventual aim of any types of waste management practices is the prevention of disease and the protection of environment.

Health aspects

In the perspectives of health, if the biomedical wastes are not treated well it may lead to nosocomial infections to hospital personnel and waste handler. Moreover, the suspended spores of pathogens may cause tuberculosis, tetanus, and other infectious diseases [18]. It has been found that use of antibiotics in human/veterinary medicine and agriculture has led to the contamination of the diverse sections of the environment including surface/groundwater, drinking water, municipal sewage, soil, vegetables, and sludge [17,19]. Once in the environment, antibiotic remains could be consumed as contaminated food and water and negatively affects the biota at different trophic levels, and on human health. Also, the plants could absorb the antibiotic residues that interfere with their physiological processes and cause potential ecotoxicological effects [19]. The presence of unused drugs and chemicals in the aquatic environment may result in cellular toxicity and antibiotic resistance of microorganisms [19,20]. Environmental effects of some of unused pharmaceutical ingredients on humans and animals has been summarized in Table 1. It has been believed that soil or aquatic productivity and associated organisms are ill affected by biomedical waste pollutants [17]. Some investigations have reported the presence of some waste chemicals in fish tissues, and their consequences on human health [21].

Table 1. Effect of unused drugs and their ingredients on to the humans and fauna (Source: [12,22-26]).

Active pharmaceutical ingredient	Known pharmacology in target organisms	Potential harmful effects on non- target organisms
Fluoxetine	Sexual dysfunction in human	Alters estradiol levels in fish
NSAIDs like diclofenac	Renal toxicity in human	Renal impairment in fish and birds, visceral gout, and death of vultures
Ethinyl estradiol	Feminization of males	Affecting fertility and development of fish, reptiles, and aquatic invertebrates
Cytotoxics	Anticancer	Reproductive toxicants and cytotoxic to fish and other aquatic species
Enrofloxacin and other antibiotics	“Growth promoters” in agriculture and poultry	Emergence of multidrug resistant strains of pathogenic organisms
Chlorpyrifos Atrazine	Pesticide	Increased susceptibility to *Ambystoma tigrinum* viral infection and increased larval mortality
Methyltestosterone	Synthetic steroid	reduced fecundity, oogenesis, spermatogenesis in snails
Cypermethrin	Ectoparasiticide	Impact on dung decomposition
Tylosin	Antibacterial	Impacts on the structure of soil microbial communities
Erythromycin, Tetracycline	Antibacterial	Inhibition of growth cyanobacteria and aquatic plants
Diazepam	Antianxiety drug	Inhibition in the ability of dissected polyps from the cnidarian *Hydra Vulgaris* to regenerate a hypostome, tentacles and a foot

Ethical aspects

It is to be expected from health care workers to keep hospitals free from blow-outing of diseases. There should be awareness among health professionals regarding influence of ill-treated biomedical waste on public health and environmental hazards. Therefore, regular training program for all the health professionals, in particular, waste handlers are utmost required to ascertain hazard free, effective management practices, which should be economically sustainable and culturally adapted in the society [24].

Environmental aspects

Improper management of wastes whether inside or outside of the hospital, paves the way for pollution of soil, water, and air. Untreated dumping of biomedical wastes promotes air pollution whereas, burning and incineration of plastics and hazardous materials associated with biomedical waste releases carcinogenic gases like dioxins and furans [23]. The diagnosis and treatment of various diseases like bone pain, thyroid glands, urinary tract infections, cardiovascular, pulmonary, digestive, central nervous systems and cancer require radioactive isotopes emitting gamma and beta rays. Such kinds of therapies, radio immune assays and research contribute to air pollution. A major drawback of this nuclear medicine practice is that these wastes are highly soluble in any environment. Therefore, it becomes difficult to store and handle as it leads to a higher risk of radioactive contamination of medical personal [3]. Poor waste management has resulted in more than one hundred million tons of plastic accumulation across the world's oceans. This plastic waste gradually broken down into smaller pieces called microplastics and nanoplastics which can cause significant damage to marine ecosystems, and negatively impact human health [27].

On the other hand, the improper dumping of wastes in low lying areas where water is stagnant, is the main causative agent for water pollution as it results in accumulation of non-degradable chemicals or radioactive substances [9]. Also, pathogens and heavy metals leached out the ground/surface water [19]. All these factors change the pH and biological oxygen demand (BOD), and overall causing water pollution. The polluted water is the sources of spread of infections by many pathogens including *Escherichia coli* and Hepatitis A virus [12,17,23]. Soil pollution could also invite infections from Enterococci, *Pseudomonas aeruginosa*, *S. aureus* and Hepatitis B virus [12]. It has been reported that the heavy metals like mercury, lead, aluminium, and cadmium could be absorbed by plants, and enter the food chain. Therefore, there is an utmost demand of an eco-friendly and easy-going techniques in biomedical waste management.

EXISTING DISPOSAL TECHNIQUES

Currently there are many techniques are in practice to dispose the waste materials as mentioned below.

Sewage/drains

This type of disposal technique is inexpensive and commonly used for liquid wastes. This practice allows human body parts or fluids and wastes to be released untreated into water. This could lead to serious health issues; hence, concurrent disinfection is required. Moreover, if such liquid waste become stagnant, will cause foul odour, and exaggerate breeding of flies and mosquitoes. Radioactive waste is generally dumped in the oceans far away from human habitations. Conventional wastewater treatment plants [WWTPs] are being employed but are unable to eliminate micro-pollutants. Thus, many of unaltered waste matematerials easily pass through the treatment processes due to their continuous introduction [17].

Incineration

This technique is a commonly employed for solid and dry waste material that cannot be recycled like by-products of medicines, surgical dressings, instruments powders, residue of decoction etc, and, disposed off in a land fill site [17]. The incineration of such a deserted material succeeds in killing of pathogens and reduction in waste mass. Although, it is an effective and hygienic way for disposal of hospital waste, it also produces ash residue which enhances the levels of inorganic salts and organic compounds by emitting high levels of various metal contaminants in the environment [10,28]. In addition, metals or plastics are also not destroyed during incineration. Generally, polymers in plastic waste are resistant to oxygen heating and explosives. Therefore, incineration which is most used in hospitals of many developing countries to take care of solid biomedical waste is not environmentally friendly [22,29]. Moreover, the air-borne by-products of incineration have venomous smell and are injurious to the ozone layer. Pest and insects produced of from ash may potentially spread disease throughout the area and damage millions of trees in both natural forests and commercial settings [30]. Moreover, the big drawback of this method is that incinerators are costly to construct, sustain and function. It consumes higher energy and requires more skilled personnel and maintenance [12]. However, an alternative method of autoclaving is used to inactivate the transmittable agents and to sterilize the equipment used in medical services [12].

Chemical Treatment

This method is employed to treat liquid biomedical waste by using calcium oxide, chlorine, and sodium hydroxide. This results in oxidation, reduction, precipitation, and pH neutralization of biomedical waste converting it into less hazardous materials [31].

Irradiation

Sometimes radiation like ultraviolet light, X-rays, gamma, and electron-beam are exploited to sterilize hospital waste. But it is a very costly method and warrants safety measures to protect workers from harmful exposure of radiation that could cause diseases like cancer [32].

Landfill/disposal

Landfill is the eventual method of disposing the incinerated material, and waste after decontaminated with above mentioned methods. On the other hand, non-hazardous waste materials are being discarded in open. Landfills are employed globally and extensively but the open dumping results in higher risks of disease transmission [9]. Therefore, landfilling should be done at locations where the ground-water level is low, and which are far from flooding sources. The solid waste from hospital is highly loaded with pathogens, animal remains, faeces, and are leached into ground water [33]. The dumped organic waste material in landfills undergoes biodegradation and decomposition in a short period of time. However, plastics and other long polymer wastes can take around ten to a hundred years to degrade in landfills processing [34]. These factors overall lead to severe pollution of ground water [17] and affect air as harmful gases like carbon dioxide and methane are being released into air from open ground [35]. Also, dumping becomes an open access to scavengers and animals that can lead to epidemic of diseases [23].

Use of bioremediation in biomedical waste management

Bioremediation is a process of breaking the toxic wastes into less toxic or non-toxic ingredients using naturally occurring organisms like microbes and plants [36]. Of the two, microorganisms are more exploited due to their ability to grow faster and be easily manipulated, thus enhancing their role as agents of bioremediation. Various groups of bacteria, fungi and algae have been employed to clean up different types of environmental pollutants [37]. Biomedical waste generated from hospital is an accumulation of liquid or solid materials comprising high amounts of organic pollutants, therefore, it could be treated biologically. And one of the encouraging biological treatments is bioremediation [38]. This technique is considered as an alternative to currently used remediation technologies including harmful chemicals and physical processes as discussed above. Bioremediation is cheaper and more sustainable method than currently existing methods which are used in disposal of the waste [1,39]. It is being used to treat polluted soil and water by changing the environmental conditions that facilitate active growth of plants or microorganisms towards degradation of certain pollutants especially biomedical wastes [12].

Microorganisms possess inherent physiological, biochemical, and genetic properties that facilitate them as ultimate candidate for remediation of pollutants in soil and groundwater. Now a days, various advanced molecular techniques have been utilized to explore the microbial population in the area needing bioremediation [36,39,40]. Moreover, use of plants in phytoremediation is recommended to degrade, eliminate, alter, or restrain toxic biomedical wastes materials present in soils, sediments, ground water and wastewater in treatment wetlands. Phytoremediation embodies an encouraging technology whereby plants and rhizopheric microorganisms offers higher potential to remediate various types of pollutants present in hospital wastes [41]. This technique is highly sustainable, economical, and competent in handling even radioactive waste from hospitals [3,42]. Scientists have found great opportunities in microbes and plants for disposal of sediments and waters impacted by nuclear waste [12,39,43-45]. It is therefore utmost important to cultivate a research approach based on bioremediation process which is inexpensive yet effective answers to treat liquid and solid hospital biomedical waste. A comparison of bioremediation with other techniques with reference to advantages and disadvantages is described in Table 2.

Table 2. Comparison of bioremediation with other techniques (Source: [1,46-48]).

Methods	Eco friendliness	Temperature	Efficiency	Byproduct	Toxicity	Expense
Sewage/drains	Not ecofriendly as untreated waste may accumulate in environment	Relies on environmental temperature	Low efficiency due to production of micropollutants, stagnant waste poses risk of human health	Open dumping results in production of poisonous gases, and mutagenic substances	Infectious and toxic materials often lead to spread of diseases	Less expensive including transportation cost
Incineration/ autoclaving	Not ecofriendly as high heat is required	High temperature is used to carry out the process	High efficiency with disadvantages of producing ashes with metal contaminants, air borne products leads to foul air	Emission of carbon dioxide, nitrogen oxides, and ashes	Highly toxic material is being released	High installation cost
Chemical treatment	Not very ecofriendly as toxic chemicals might be required	Temperature requirement varies according to types of chemicals used	Medium efficiency with risk of chemical exposure to workers	Plastic bags, chemical oxides	Highly toxic chemicals are used	Not expensive
Irradiation	Not ecofriendly as radiation could leaked out to cause various diseases	High temperature in a controlled condition	Low efficiency with risk of radiation exposure to workers	Production of mutagenic substances	Less toxicity	Less expensive
Disposal/ landfill	Not ecofriendly as leachate could pollute ground water, release of harmful gases and danger of spreading epidemics	Very low temperature is needed	Medium efficiency with probability of disease transmission, polluting ground water or air.	Leachate, metals, glass, carbon dioxide, plastics	Toxicity relies on the landfill material	Less installation cost
Bioremediation	Ecofriendly being a natural and sustainable process. The treatment products are harmless cell biomass, water, and carbon dioxide	Needs less effort and could be carried out on site under natural environment	High efficiency with complete degradation of contaminants, no use of dangerous chemicals, and continuous site use.	No harmful byproducts, completely biodegradable material is produced like water, carbon dioxide and inorganic substances	No toxicity, conversion of harmful chemicals into water and harmless gases, contaminants are destroyed, not simply transferred to different environments	Simple, less labor intensive and cheap due to their natural role in the environment

Microbial remediation

A microbial remediation approach depends on microbial enzymes to degrade organic hydrocarbons into less hazardous material. The main advantage of this process is complete mineralization of the organic compounds into carbon dioxide and water. Microbes exploit pollutants as their sole carbon source and transform the contaminants by co-metabolic pathways [49]. There are three phases of biodegradation (i) Natural attenuation that involves reduction of pollutants by natural microorganisms (ii) Biostimulation, a technique to enhance the biodegrading efficiency of microorganisms by supplying more nutrients and oxygen to the process (iii) Bioaugmentation, where more efficient supplementary microorganisms are added to the existing natural microflora to target the specific contaminants [50]. Several factors, such as pH and temperature of the surrounding environment, aerobic or anaerobic conditions, and nutrient availability in the form of nitrogen and phosphorus content, all influence bioremediation for better outcomes [49]. Several mechanisms/pathways have been reported for the biodegradation of a variety of organic compounds by microorganisms such as biological oxidation and hydrolysis [38,49]. Among the various microorganisms, the non-pathogenic microbes are employed in hastening the degradation of biomedical wastes by restricting the accessible nutrients and suppressing the growth of pathogenic microorganisms [38]. *Bacillus*, *Flavobacterium*, *Nocardia, Pseudomonas*, *Rhodococcus*, *Sphingomonas*, and *Mycobacterium* are capable of degrading aerobically a variety of complex organic compounds [51]. Whereas *Aeromonas, Pseudomonas*, and sulfate-reducing bacteria are being used in the bioremediation process under anaerobic conditions [52]. Hydrolytic bacteria have been reported to reduce the parameters of organic wastes in polluted water. Liquid biomedical waste reservoirs containing wreckages of diverse sorts of organic matters are found to be a deep source of these bacteria. Ethica and coauthors [53] have reviewed the exploitation of hydrolytic bacteria in remediating the biomedical wastes that has significantly been increased in the hospitals in Indonesia including Central Java Province. Therefore, use of hydrolytic bacteria as bioremediation agents could be an encouraging strategy to resolve the problem of disposal of liquid biomedical waste.

Bioremediation of emerging contaminants and microplastics

Pharmaceuticals, plastic polymers, personal care products [PPCPs], pesticides, and heavy metals are distinct group of chemicals, referred to as emerging contaminants because of their intrinsic potential to induce a variety of physiological effects in humans [54]. Microbial cells are the best choice for degradation of such types of pollutants, as they possess a high surface-volume ratio, show reduction in the time of biomass transformation, higher metabolic rate and could be easily sterilized [55]. However, a range of bacteria, fungi, and plants have been reported to be involved in the biodegradation of toxic organic pollutants through secretion of enzymes; yet fungi are particularly promising candidates [54]. Fungi have been shown to break down a variety of pharmaceuticals ranging from antibiotics [56], anti-inflammatory drugs [57], anticancer drugs [58], antidepressants [56], diuretics [59], analgesics [60] and beta-blockers [61]. Wetzstein and coauthors [62] have reported transformation of enrofloxacin and other antibiotics by *Basidomycetes*.

Nowadays, use of plastics in our daily life activities is increasing in the form of packaging in different industries for food, brewing, cosmetics, pharmaceutical, and other production sectors where there is a need to pack their end products for efficient and safer product's delivery to the community [63]. Conventional plastics are synthetic polymers produced through the biochemical process of polymerization or polycondensation and when degraded, results in microsized plastic [diameter <5 mm] termed as microplastics [MPs]. These are considered as 'contaminants of emerging concern' and are added to environment through various sources including cosmetic products, drug carriers, glitters, and degradation of larger plastics in the form of water bottles and fishing net [64]. MPs have negative effects on humans and animals such as causing damage to esophagus, intestinal obstruction, reduced reproduction, and disorders of metabolism and decreased immune response [63,64]. *Aspergillus*, *Penicillium* and *Trichoderma* are well known taxon groups of plastic degraders [65-67].

Cleaning of microplastics

Various chemical and biological approaches are employed in degradation of plastic, but from ecofriendly way biological approaches are more common. This involves use of microorganisms in hydro-biodegradation and oxo-biodegradation of the polymers followed by photo degradation and chemical degradation. Recently, Alnahdi and coauthors [2023] have presented a concept of engineering a microbial ecosystem, termed the microbiosphere. to design a novel microbial ecosystem engineered as a bioremediation tool to get rid of the ocean of micro- and nanoplastics [27]. Various research has shown that different groups of bacteria, fungi and actinomycetes possess unique property of degrading molecular chains in polymers of both natural and synthetic plastics by converting non-biodegradable plastics into low molecular weight polymers, CO_2, water, biogases like methane and other less harmful components [68]. Extracellular and intracellular depolymerase enzymes are involved actively in natural degradation of polymers. Polyethylene terephthalate [PET] is one of the examples of petrochemical-based plastics. The identification of *Ideonella sakaiensis* 206-F6T signified another scientific development in bioremediation of PET [69].

Degradation of recalcitrant pollutants in soil by microorganisms

Secretion of intra and extra cellular enzymes in bacteria and fungi makes them the ultimate degraders of recalcitrant organic matter and lignin and organo-pollutants in soil [54]. A variety of microbial enzymes secreted are basis of bioremediations as briefly described here. The oxidoreductases through oxidative coupling carry out degradation of xenobiotics such as various phenolic substances [70]. One of the most abundant recalcitrant wastes like chlorinated phenolic compounds are degraded due to the action of extracellular oxidoreductase enzymes, like laccase, manganese peroxidase, and lignin peroxidase, released from fungal mycelium [71]. Halogenated organic compounds are degraded by specific oxygenases. Biodegradation of various aromatic and aliphatic compounds are catalyzed by monooxygenases. The catechol dioxygenases found in the soil bacteria are involved in the transformation of aromatic precursors into aliphatic products [70]. Intra and extracellular laccases produced by many microbes make them capable of catalyzing the oxidation of ortho and paradiphenols, aminophenols, polyphenols, polyamines, lignins, and aryl diamines as well as some inorganic ions [72].

On the other hand, eradication of soils contaminated with hospital solid waste especially radionuclides are done by digging and transporting it to a distant waste disposal site, but it is very costly [73]. Bioremediation via microorganisms could be a striking substitute to mining contaminated soil [45]. Microorganisms such as *Desulfuromus aferrireducens* and *Rhodanobacter* sp. have been reported to interact with these contaminants [74,75]. Researchers have attempted to create native or genetically engineered microbes for the remediation of hospital waste contaminants including radionuclides [39,76]. It has been found that remediation by microbes can affect the solubility, bioavailability, and mobility of radionuclides [8]. Several methods of microbial remediation have been employed, especially for remediation of organic recalcitrant pollutants including heavy metals and radionuclides as depicted in Figure 1 and Figure 2 and as discussed below.

Biosorption and biostimulation

Biosorption is a process that utilizes negatively charged cell membranes and polysaccharides secreted on the outer surfaces of bacteria as adsorbents to seizure the positively charged metals [39,45]. Multiple number of mechanisms and interactions for sorption of metals to intact cells are predicted but not yet completely understood [8,53]. Khani and coauthors [77] reported that the brown marine alga *Cystoseira indica* could show the adsorption of radionuclide U[VI] and, also observed that the pre-treatment of the alga with calcium could increase the adsorption efficacy of several radionuclides. Moreover, various other microorganisms such as *Citrobacter freudii* and *Firmicutes* have been reported to absorb radionuclides [78,79]. Biostimulation is also used to augment the bioremediation of radionuclides [42]. In a study from Vrionis and coauthors [80], an *in-situ* remediation method was established to diminish the bioavailability of uranium in ground water, and to prevent its the further leach out by stimulating the activity of dissimilatory sulfate- and iron-reducing microorganisms.

Biomineralization

Biomineralization is a process by which mineral crystals are accumulated in the matrix of living organisms. Microorganisms can easily interact with metal ions and immobilize them to form biofilms to bind significant amounts of metallic ions, which can make a platform for the precipitation of insoluble minerals [44]. *Citrobacter* sp. have been reported to enzymatically accumulate metal phosphates. It has been found that polycrystalline NaUO2Po4 could assemble in and around the cell wall of *Citrobacter* by sorption to lipopolysaccharides and acid phosphatase of an outer membrane. The mineral formation is accelerated by an incoming UO4 and an outgoing PO4 gradients resulting in total removal of U from the solution and binding of 1 mg NaUO2Po4 per mg of the cell [8,81].

Genetically modified microorganisms

Researchers can apply a combination of genome-based experimental and modelling techniques on microorganisms that are culturable and have significance in bioremediation to evaluate their physiology [76]. Moreover, modern environmental genomic techniques have made it possible for related studies on uncultured organisms as well [82].

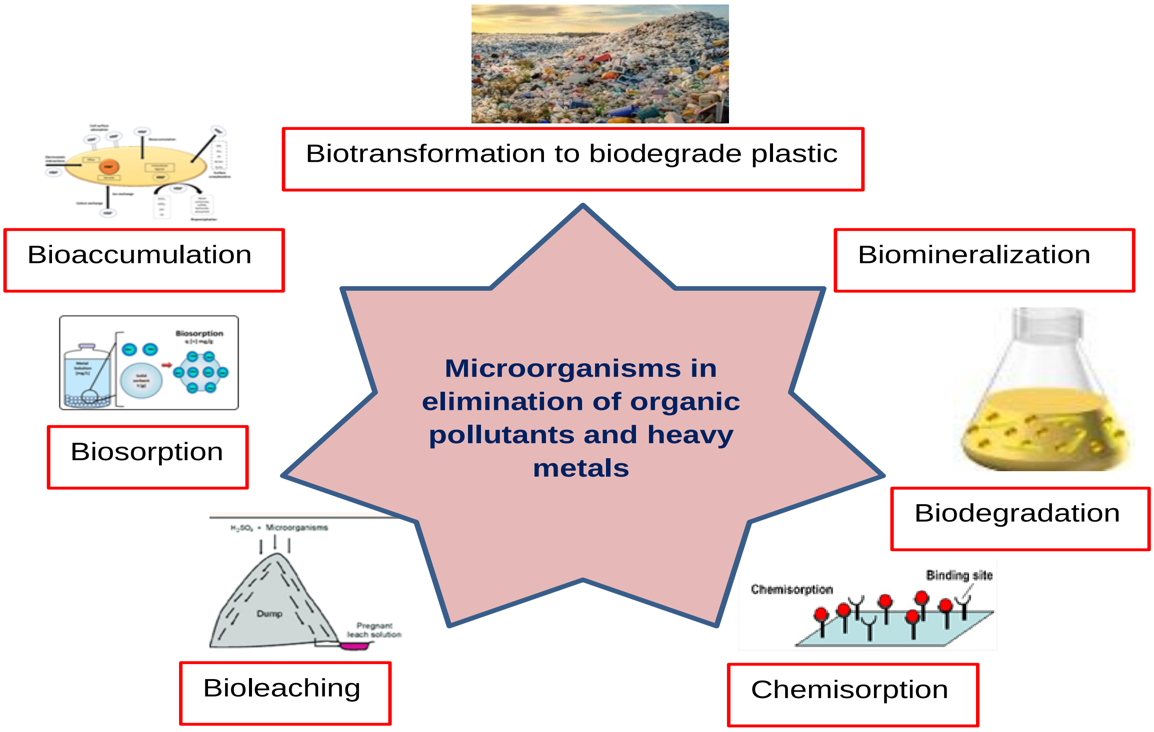

Figure 1. The process of bioremediation of organic pollutants and heavy metals by microorganisms.

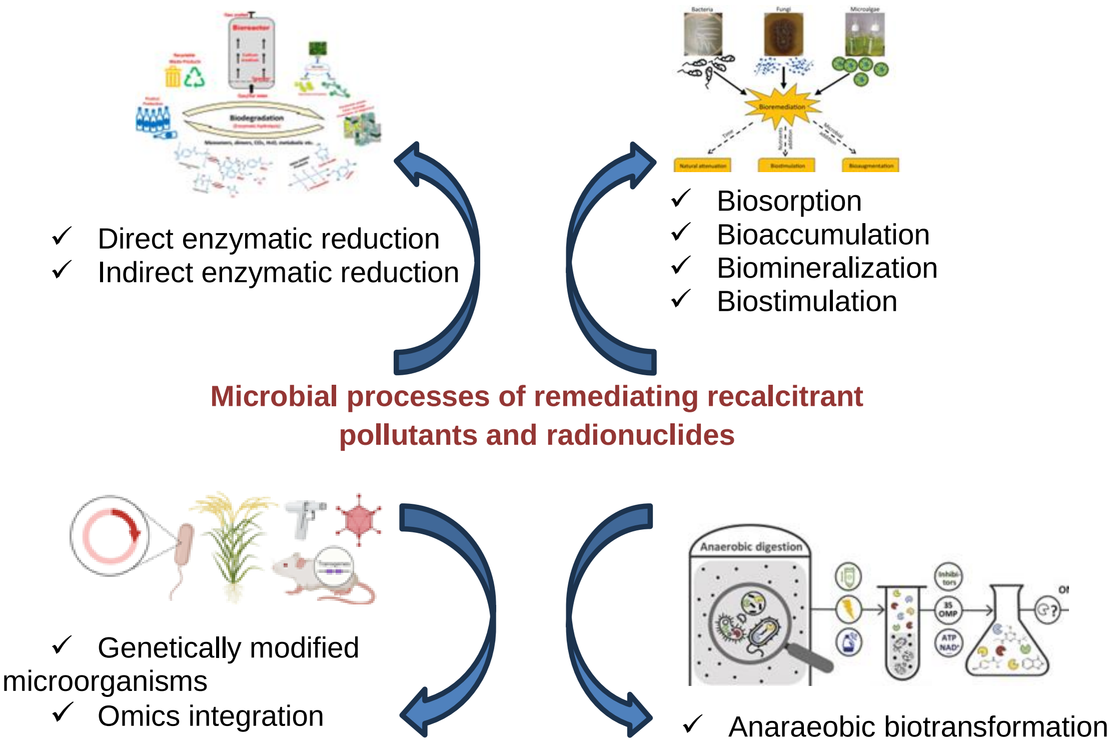

Figure 2. Mechanistic approach of microorganisms in remediating recalcitrant pollutants including radionuclides.

Therefore, it has been becoming possible to combine models predicting the activity of microorganisms employed in bioremediation with models highlighting existing geochemical and hydrological properties to convert bioremediation from a largely pragmatic exercise into a science [39,76,82,83]. Using genetic engineering and recombinant DNA technology, many character-specific microorganisms have been developed for efficient elimination of metal by sorption. For example, distinct protein constructs have been created in which the bacterial cell surface is furnished with metal binding polypeptides by fusion-binding domains to outer-membrane-anchored proteins that include metallothioneins [84], randomly produced polypeptides [85], polyhistidines and synthetic phytochelatines [85,86]. These protein constructs demonstrated an increase in metal binding as metallothioneins were examined in microcosm field study [87]. Another methodology has also been endeavoured to increase the metal accumulation by blending the specific metal transporter with metallothiones in the cytoplasm [88].

Beckwith and coauthors [89] have generated a recombinant strain of *E*. *coli* displaying five times the sorption aptitude for U[VI] radionuclides by modifying the transporter genes *nixA* [*Helicobacter pylori*] and *merTP* [*Serratia marcescens*], respectively. Therefore, it was proposed that the expression of both metal transporter proteins and metal-binding peptides may augment a strain's capability to accumulate metal ions. Whereas the interaction of site-specific microorganisms starts solubility of altered radionuclides by addition or removal of electrons [42]. This would raise the mobility of the contaminant and would allow it to be easily cleansed from the environment [74]. This microbially facilitated remediation displays possibilities for bioremediation of radionuclides in the environment, either to immobilize them in place or to pace up their removal. A discussion follows of '-omics'-integrated genomics and proteomics technologies, which can be used to track down the genes and proteins of importance in a given microorganism in the direction of a cell-free bioremediation approach [8,82,83].

Limitations of microbial remediation

Bioremediation is restricted to biodegradable compounds and is a highly specific process. Success of this approach depends on metabolic ability of microbial populations accompanied by optimum environmental conditions of nutrients and contaminants [48]. Also, challenges are being faced to scale up bioremediation process from batch/pilot scale studies to large scale field operations. Therefore, more advanced research is needed to develop bioremediation technologies suitable for sites with composite combinations of contaminants. Furthermore, bioremediation might take longer time compared to other methods as there is no acceptable endpoint for bioremediation treatments [46].

Phytoremediation

Now a days, phytoremediation is developing as a cost-effective means of treatment of wastes. The use of plants offers numerous remarkable gains compared to the currently practiced in situ and ex situ technologies of soil remediation [36]. Phytoremediation benefits in terms of low investment and maintenance costs, simple start-up, non-intrusiveness, superior public acceptance, and the lovely landscape that arises as a finishing product [39,90]. Also, this technique is unbiased in terms of production of carbon-dioxide. As the harvested plant biomass upon burning does not release extra carbon dioxide into the atmosphere outside what was originally embraced by the plants during growth [90]. Applications of phytoremediation are being verified for cleaning up contaminated soil, water, and air especially polycyclic aromatic hydrocarbons, organic matter and hospital wastes [3].

Various types of strategies are being adapted for phytoremediation as summarized in Table 3 and mentioned briefly here. (i) Phytoextraction; removes metals and organics waste from soils by assembling them in the biomass of plants (ii) Phytodegradation or phytotransformation; is the usage of plants to consume, reserve and degrade the organic pollutants (iii) Rhizofiltration; comprises the removal of pollutants from aqueous sources by plant roots (iv) Phytostabilization; reduces the bioavailability of pollutants by immobilizing or binding them to the soil matrix (v) Phytovolatilization; is the utilization of plants to intake pollutants from the growth matrix, modify them and release them into the atmosphere [91,92]. However, scientific and industrial interest in phytoremediation now is largely emphasized on phytoextraction and phytodegradation utilizing preferred plant species grown on wastelands. These plants are harvested to eliminate the plants together with the accrued waste material in their tissues. Depending on the kinds of pollutants, the plants can either be disposed of or utilized in other processes, such as burning for energy manufacture. In principle, phytoextraction eradicates toxic substances from contaminated soils, distillates them in biomass and concentrates the waste product by combustion [39,93].

Table 3. List of various applications of phytoremediation process (source: [3,39,41,94]).

Application	Description	Contaminants	Types of plants
Soils			
Phytotransformation	Sorption, uptake, and transformation of contaminants	Organics, including nitroaromatics and chlorinated aliphatics	Trees and grasses
Rhizosphere biodegradation	Microbial biodegradation in the rhizosphere stimulated by plants	Organics, e.g., PAHs, petroleum hydrocarbons, TNT, pesticides	Grasses, alfalfa, many other species including trees
Phytostabilization	Stabilization of contaminants by binding, holding soils, and/or decreased leaching	Metals, organics	Various plants with deep or fibrous root systems
Phytoextraction	Uptake of contaminants from soil into roots or harvestable shoots	Metals, inorganics, radionuclides	Variety of natural and selected hyper accumulators, e.g., *Thalaspi, Alyssum, Brassic*a
Water/groundwater			
Rhizofiltration	Sorption of contaminants from aqueous solutions onto or into roots	Metals, radionuclides, hydrophobic organics	Aquatic plants [e.g., duckweed, pennywort], also *Brassica*, and sunflower
Hydraulic control plume capture/phytotrans	Removal of large volumes of water from groundwater and/or aquifers by trees	Inorganics, nutrients, chlorinated solvents	Poplar, willow trees
Phytovolatilization	Uptake and volatilization from soil water and groundwater; conversion of Se and Hg to volatile chemical species	Volatile organic compounds, Se, Hg	Trees for VOCs in groundwater, Brassica, grasses, wetlands plants for Se, Hg in soil/sediments
Vegetative Caps	Use of plants to retard leaching of hazardous compounds from landfills	Organics, inorganics, wastewater, landfill leachate	Trees such as poplar, plants such as alfalfa and grasses
Constructed wetlands	Use of plants as part of a constructed ecosystem to remediate contaminants from aqueous waste waters	Metals, acid mine drainage, industrial and municipal wastewater	Free-floating, emergent, or sub-mergent vegetation; reeds, cattails, bamboo

For the last several decades, phytoremediation is being exploited to clean up a range of organic and inorganic pollutants such as agrochemicals [95], chlorinated solvents [96], heavy metals [97], polycyclic aromatic hydrocarbons [98,99], polychlorinated biphenyls [100], and radio nuclides [42]. These soluble organic/inorganic pollutants, which move into plant roots or rhizosphere by the mass flow route of diffusion, seem to be highly open to the remediation procedure [41]. It has been observed that plants and rhizospheric microbes are able to convert some toxic chemical compounds to some degree [39,45].

Some radioactive isotopes as actinium [Ac], barium [Ba], radon [Rn], and some other rare elements are shown to be accumulated by plants such as *Dicranopteris dichotoma, Japonica gleichenia*, and *Struthiopteris niponica* [101]. In a study from Isaura and coauthors [3], *Phragmites australis* has been found to accumulate heavy metals and radioactive compounds such as iodine-131 at root level. This plant is broadly recognized for its hyper accumulating ability towards heavy metals and lixiviates. It is also employed in artificial wetlands to handle the industrial discharges. *P. australis* has been shown to accumulate chromium, copper and zinc on the stem and rhizomes, and nickel at foliar level [102].

Interactions between plants and microbes

In addition to sequestration of pollutants, the plant roots may surge degradation of waste material in situ through their root structures. Plant roots and their exudes are responsible for increasing the microbial strength in the soil surrounding by a greater degree, thereby increasing microbial activity [95,97]. Moreover, the metabolic requirements for pollutant degradation could also direct the types of formation of the plant–bacteria interaction i.e., specific, or non-specific [36,41,95]. Plants and bacteria undergo in a specific relationship surrounding the rhizosphere, where plant roots provide carbon source to the bacteria to bring down the phytotoxicity of the contaminated soil [41]. Also, plants and bacteria undergo nonspecific associations in which regular plant processes excite the microbes to degrade the wastes pollutants in the course of normal metabolic activity in soil [41,92]. In return, bacteria can boost the ability of plants to degrade toxic substances or diminish the phytotoxicity of the polluted soil [98,103]. The fundamental idea to this association is that the plant adjusts its behavior in contaminated soil to kindle the microbial communities that degrade contaminants [40]. The specificity of the plant–bacteria interaction is reliant on soil conditions, which can modify contaminant bioavailability, conformation of root exudates and nutrient levels [104].

Plants generate specific signals in reaction to specific pollutants resulting in bacteria to detoxify the harmful waste in soil and the plant delivers root exudates as energy source or in other way to intensify the detoxification activity by the microbes in the rhizosphere [103]. It is fact that plants encountering toxic compounds in soil would not be able to survive unless they can discover a tactic to detoxify the contaminant. Recently, a study had shown the exploitation of plant growth promoting rhizobacteria (PGPR) strains as a strong candidate to assist *Sesbania sesban* growth under heavy metal stress conditions [105]. Therefore, plants have evolved ways of manipulating rhizobacteria as a method to detoxify toxic substances in soil [106].

Limitations of phytoremediation of landfill sites

A major disadvantage of phytoremediation process is its relatively slow speed compared to conventional cleanup technologies. It takes quite a few years or even decades to significantly reduce the level of toxic substances in soil [92]. Excavation/landfill, or incineration take several weeks to months to complete the cleanup process but phytoextraction may require several years [33,90]. In fact, the successful utilization of phytoremediation relies on the growth of the plants. A very high concentration of toxic substances could hinder plant growth, therefore, its application on some sites or some parts of sites could be restricted. Hence, sites with medium levels of toxic substances spread widely within the root zone are especially preferred for phytoremediation procedures [41]. Therefore, plant scientists are taking up the challenge to enhance the performance of plants in eliminating highly toxic substances from the soil without affecting its growth and efficiency. It necessitates further need of developing more research and acquiring expertise on the ecological decontamination mechanisms of plants. If genetic engineering is becoming successful in generating plants being able to recover contaminated lands in convenient time period, then we would see a superior public approval of phytoremediation with respect to the environmental safety [91,107].

Potential alternative methods to be adapted in clean-up of waste

Now-a-days, the pharmaceutical industry is implementing the several ‘Green Chemistry’ practices by curtailing the usage of reagents that are perilous to the environment and trying to come up with unconventional methods [108]. Many eco-friendly measures can be adapted in the handling of biomedical waste as follows.

Reduce, reuse and recycle

This approach comprises of the processes and policies of decreasing the quantity of waste generated by a person or hospital. Like use of a variety of devices for diagnosis, treatment and other activities should be appropriately established to endure sterilization. If glycerine syringes are sterilized properly, these could be given to the same patient again [12]. On the other hand, the water as effluents from treatment plant could be used for agriculture, construction, dust control, landscape, toilet flushing, and several other activities. The advancement of recycling technologies and the reuse of ash produced from incineration of biomedical waste in different systems can overcome the problem of space limitation. Several studies have reported successful use of biomedical waste in agriculture and construction sectors to reduce the leaching of its harmful elements into the environment [12,13,28]. Recycling reduces pollution in all the ecosystems, requires less energy, helps in natural conservation, and saves fast-depleting landfill space. The idea of transforming waste into energy is earning recognition now-a-days. Bio-methanation, has a great potential for making of energy from organic wastes, which aids to lessen the consumption of fossil fuels and carbon dioxide emission. Studies have also highlighted that wastewater can be used to produce electricity and disinfectant [12,109]. Moreover, plastics wastes can be recycled for construction of roads. It exploits bottles and other plastic materials that can be melted and transformed into other products like plastic tables and chairs [12,110].

Solar energy in waste management

It is quite interesting to employ solar energy to disinfect infectious medical waste in developing countries as it is a cheaper approach. Solar energy can be exploited to power the autoclave and designed as a suitable method to be implemented in waste management especially in a small hospital set-up. Several studies have reported that use of solar disinfection with lime stabilization process exhibited a noteworthy drop in the parameters like alkalinity, chemical oxygen demand, electrical conductivity, total solids, volatile solids, and microbial colony count at different stages of disinfection. These observations indicate that pathogens of biomedical waste can be efficiently wiped out using this approach [111,112].

CONCLUSION

The unorganized disposal of used or expired pharmaceutically active compounds, other hospital wastes including plastics, heavy metals and organic pollutants poses a serious threat to the aquatic and terrestrial ecosystem. Therefore, an aappropriate biomedical waste management strategy is considered as the key asset of the hospital sanitation and its maintenance activities. Biomedical waste treatment is a global issue and research is going on to find out inexpensive and environmentally friendly techniques to deal with such types of waste as the preexisting non-bioremediation methods are considered costly and environmentally unfriendly. In particular, the insufficient management of heavy metals, plastics and radioactive waste is a problem that encourages the need for more sustainable alternatives for its final disposal. Bioremediation has such a potential to restore contaminated environments inexpensively yet effectively. The understanding of the dynamics of bioremediation requires a multi-disciplinary tactic comprising the biology, biochemistry, and engineering of remediating systems. Natural attenuation by native microorganisms, biostimulation and bioaugmentation are the processes employed to degrade the target contaminant. However, the paucity of knowledge about the factors regulating the growth and metabolism of microbes in polluted environments often restricts its execution. Use of novel molecular tools and modeling technologies have enabled researchers to evaluate physiology of microorganisms in mineralization of pollutants by improving their neutralization efficiency. Moreover, cost effective, eco-friendly and highly efficient technology capable of eliminating plastics are of great environmental interest. Microorganisms are the most effective agents for the biodegradation of polymers and there is an increasing demand to explore their ability to grow in different environmental stress conditions to use carbon from the plastic polymers as an energy source. There are several benefits of recycling plastic waste like the protection of human life by decreasing carbon dioxide and other harmful gases in the atmosphere, which can occur during incineration or combustion of these wastes. Thus, employing microorganisms to detoxify the pollutants enhances sustainable biodegradation, improves water quality, and ensures eco-friendly alternative bioremediation strategy. Phytoremediation is possibly a cost-effective technology as the resulting biomass can be used for production of heat and energy and can be used in various specialized commercial facilities. Therefore, it could become a new environmentally friendly kind of technology. Although, rapid progress in the understanding of bioremediation is on the horizon. Research on biomedical waste management using bioremediation processes should be constantly done as the growing number of hospitals needs more effective and efficient treatment means.

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