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Pharmaceutical Waste Treatment and Disposal of Concentrated Rejects: A Review

Parimal Pal* and Ritwik Thakura
Environment and Membrane Technology Laboratory, Department of Chemical Engineering
National Institute of Technology Durgapur, India

Abstract
Efficient treatment of pharmaceutical waste is a big challenge because of the enormous quantity, complexity and hazardous nature. Lack of implementation of effective treatment technology aggravates the situations further in the countries facing the challenges of rising population, increasing urbanisation and industrialization generating enormous quantities of industrial wastes. This paper critically reviews the existing practices to suggest the best options. While the slow biological treatment schemes often fail to sustain microbial activity in presence of toxic components in concentrations, the other physico-chemical schemes often fall short of meeting the stringent regulations of waste discharge and disposal. Thermal incineration approach for sludge disposal has never been environmentally justified because of release of dioxin and indirect transfer of obnoxious substances. Emerging membrane-based schemes can be very compact, eco-friendly, small, flexible, economically viable, easy to install, operate and maintain.

Keywords: Pharmaceutical wastewater, Conventional treatments, Emerging technologies, Membrane separation.

1.0 Introduction
Effective treatment of pharmaceutical waste is a big challenge because of the enormous quantity, complexity and hazardous nature. The pharmaceutical wastes comprise of drug residues with high biological oxygen demand (BOD), chemical oxygen demand (COD), pharmaceutically active compounds like hormones, antibiotics (PhACs), toxic substances, surfactants and volatile organic compounds (VOCs) which constitute potential threat to biosphere. Many of these pharmaceutical wastes pose serious threat to human health and ecosystem because of their continuous accumulation in the ecosystem leading to even development of antibiotic-resistant microbial strains. The pharmaceutical industries across the world indiscriminately generate huge quantities of pharmaceutical wastes [1]. So, the effective management and disposal of these wastes generated poses a veritable challenge before the scientific community especially because of the presence of pharmaceutical residues in the outlet of the conventional wastewater treatment facilities. The term "pharmaceutical wastewater" mainly refers to the effluents and wastes generated during manufacturing of pharmaceuticals. However, alarming rate of disposal malpractices of unused medicines from hospitals and households [2- 4] has made them a potential source of pharmaceutical waste. Pharmaceutical wastewater thus should include waste from pharmaceutical industry as well from houses and hospitals which contaminates the environment. Table 1 describes the various constituents of pharmaceutical wastewater.

A big problem frequently encountered in handling pharmaceutical wastewater is its highly variable nature as the composition of the raw materials varies widely for one class of products to another. Many pharmaceutical companies use pretence of confidentiality of composition to escape from the regulations of stringent pollution control norms. Thus without completely revealing the magnitude and nature of the toxic substances they continue to release pharmaceutical wastes to the environment. Often illogical mixing of industrial effluents, domestic sewage and hospital wastes in the public sewer handling facilities blows the problem out of proportion.

Generalization in treatment approach in this case turns difficult because of poor empirical relations of pharmaceutical compounds, wastewater characteristics (viz., COD, BOD, TSS, TP, and OIL) and the operational parameters of flow and hydraulic retention time (HRT) [5]. This further complicates the treatment

process. This is perplexing because there are studies that indicate very high (80- 100%) removal of pharmaceuticals like ibuprofen, ketoprofen, indomethacin, acetaminophen, and mefenamic acid achieved over a solid retention time of around10 to 20 days [6]. On the other hand, reappearance of traces of pharmaceutical and personal care products in the treated water samples from the wastewater treatment plants (WWTP) points to the failure of these facilities in complete removal of the persistent compounds [7]. Another wrong approach in handling pharmaceutical wastewater is it's mixing with sewage water or even mixing with waste streams discharged from different unit operations. Such mixing results in very complex wastewater difficult to administer and treat effectively. Attempt to isolate the components for recovery turns the overall treatment quite expensive. While individual treatment strategies turn ineffective, it introduces unknown problems and new types of wastewater whose treatment and disposal measures are largely unmitigated. Under this perplexing situation, revisiting the existing treatment technologies and the prevalent practices of handling pharmaceutical wastewater is absolutely necessary so as to come out with clear suggestions towards formulation of best strategies and directing research for developing sustainable technologies.

1.1. Pharmaceutical wastewater: composition and classification

The pharmaceutical industry wastewater can be classified roughly according to their sources as: a) municipal wastewater, b) spent liquors from fermentation process, c) chemical wastes, d) condenser wastes from evaporation and e) floor and laboratory washing waste. Biotechnological production of pharmaceuticals leads to discharges of chemicals used as ancillary substances like buffers, chelator and antibiotics into the aquatic environment. Recent studies have indicated that 15–20% of medicines used in hospitals are potentially bio-accumulative. To add to this is the pseudo-persistence and eco-toxicological impacts of continuous discharge of pharmaceutically active compounds (PhACs), the main noxious constituents. PhACs are complex molecules most of them being polar in nature with molecular weights ranging from 200 to 500/1000 Da. They are widely used due to specific biological activity which aids in the application of the drugs. Table 2 presents the composition of pharmaceutical wastewater when classified with respect to different constituents arising from different sources [8-10]. In order to access the available pharmaceutical waste treatment methods and to develop a comprehensive policy to discharge minimal waste in environmentally benign manner, pharmaceutical wastes may be divided into two categories:

a) waste generated by the medicinal companies and the secondary wastes obtained from treatment and recycling plants;
b) medical waste from hospitals and the domestic sector which substantially contaminates the sewers.

The second category of wastes are the sources that contribute towards active pharmaceutical residues in public sewers and subsequently in the municipal wastewater treatment facilities that are commonly ill-equipped to deal with such specialized wastes.

1.2 Hazards mapping and international directives

Active pharmaceutical ingredients (API's) and the bacteria and fungi that grow on the residues can be highly deleterious. Therefore, environmental risk assessment prior to obtaining marketing authorization of pharmaceuticals for human use as has been stipulated by the European Medicines Agency (EMA) since 2005 is a must (EMEA, 2006) [11]. In this context, hazard mapping and surveys to investigate the eco-toxicological levels assume significance as such investigations in many cases have indicated great risk of the workers involved in waste handling against the deadly diseases like lung and skin cancer, bronchitis, tuberculosis and a host of other such ailments [12, 13]. Evidence suggests that presence of ketone group is one of the main eco-toxicity contributors. Contribution of molecular and structural fragments in increasing toxicity in the environment has been established with the help of quantitative interspecies toxicity correlation models for structurally diverse pharmaceuticals (especially for fish) [14]. It is very important to know the detrimental effects of such toxic compounds to marine population and small organisms residing in the soil as have been illustrated in some studies [15-16]. The WHO directive clearly lays permissible amounts of different compounds in the environment and health risks posed by exposure to Active Pharmaceutical Ingredients (API) even when present in very dilute concentrations. Researchers explicitly measured damage caused to the

environment like sharp decrease in vulture population in the Indian subcontinent due to exposure to diclofenac (an anti-inflammatory drug) [17], sensitivity of blue-green algae towards antibiotics, untreated residues of Fluoroquinolone contributing to evolution of Fluoroquinolone-resistant *Campylobacter jejuni* (an important human pathogen) [18], their entry into trophic level of food chains and their potential to bio-accumulate among several others. Resistant stocks of API's have affected the breeding of zebra fish and long tailed rainbow trout. Often ignoring pollution associated with waste volume minimization practises led to the creation of secondary pollution sources. The leachates, fumes, water soluble compounds present are responsible for widespread degradation of the environment [19-21] impairing soil quality, groundwater, water bodies and air quality together.

1.3 Effectiveness of the prevalent strategies

Pharmaceutical wastes continue to pose big treatment challenge largely because of adoption of wrong or faulty approaches and ineffective methodologies as significantly revealed in quite a few studies [22-25]. Amidst such wrong approaches, irresponsible and indiscriminate flushing of millions of tons of unused medicines continues unabated which invariably find their way into the municipal wastewater systems. This leaves potential risk of adding to the levels of hazards through BOD and toxic COD loadings. Though the developing countries are touted as potential pollution hotspots Europe is the second largest contributor of pharmaceutical residues. Many of the pharmaceuticals that are discharged into water bodies are not readily degraded and they are potential threat to the biosphere as their continuous release makes them semi-persistent as evident in the findings of some research [26]. Pharmaceuticals are potentially dangerous environmental contaminants because of their interference with biological processes even at extremely low concentrations [27]. Another major concern in effective treatment has been the lack of administering treatment stages with respect to the toxicity levels during each stage of treatment. This is an important issue as the total toxicity of pharmaceutical wastewater rises due to chemical reactions and mixing of substances that could have been separated. Even inside a pharmaceutical industry, it is extremely undesirable that wastes from different segments are allowed to mix because wastes differing in physical and chemical characteristics interact with each other creating a complex hybrid wastewater with properties that pose even greater difficulty in analysis, handling, isolation of the components and overall treatment. Illogical method of disposing industrial effluents, domestic sewage and untreated hospital wastes together in public sewer handling facilities only aggravates the problem.

1.4 Treatment methods

1.4.1 Autoclaving

Autoclaving includes a high temperature treatment of the wastes to degrade noxious chemicals and microbes that grow on them. The residues of antibiotics often bear high organic loadings that can be treated using autoclaves. Despite high efficiency (>98%), autoclaving or supercritical fluid carbon dioxide sterilization [36] needs subsequent treatments and is at present quite unaffordable because of involvement of high cost. Therefore, the major challenge is to develop a technology that is economically viable and practically feasible. If the economic factor is not taken into account these methods will simply be inconsequential to millions of people in the developing countries where medicinal waste volume is very large.

1.4.2 Physico-chemical methods

Physico-chemical methods like ion–exchange, adsorption, coagulation-flocculation, frothing, precipitation, chemical reduction, electrochemical processes [37] as well as the combinations of these processes [38] are used to treat wastewater in different stages right from initial production to finally handling their cumulative toxic concentrations in assorted sewage. The efficacy of these conjugate processes lies in their success where direct physical or chemical treatments is not suitable for handling medicinal wastewater owing to their poor efficiency in removing dissolved COD and introduction of complex chemicals to the system [39]. It has been observed that while processes like precipitation-air floatation show a higher COD removal efficiency over coagulation–precipitation process; the latter involves less operating costs (almost 25%) than the former.

Comparison of relative potential of flocculants (ferric chloride, calcium oxide, chloride and calcium hydroxide) to remove phosphorus from a predominantly phosphorus bearing wastewater shows that removal rates of the flocculants are dependent on concentration as well as pH [40, 41]. The diverse nature of the pharmaceuticals makes them treatment-specific for instance; investigation of the principal removal mechanisms of Fluoroquinolone suggested adsorption of sludge and/or flocks is more effective than biodegradation [42, 43]. The treatment options under this category are subdivided in to the major categories as detailed in the subsequent sections where references connected to significant breakthroughs only have been considered.

1.4.3 Advanced oxidation processes

Advanced Oxidation Processes (AOPs) include a class of treatments that include heterogeneous and homogenous photocatalysis based on near ultraviolet (UV) or solar visible irradiation, electrolysis, ozonation, ultrasonication (US), wet air oxidation (WAO) and Fenton's treatment. The emerging processes include ionizing radiation and treatment subjecting to microwaves and pulsed plasma. The AOPs utilize specific features of the oxidizing agents in degrading the PhACs. Some research studies [3, 44-45] have established that such AOPs can be very effective particularly in treatment of persistent pollutants or drugs such as carbamazepine. Mechanisms of degradation may vary from treatment to treatment. For example, in ozone-based advanced oxidation process, lytic activity of ozone is used to simultaneously digest and remove personal care products. On the other hand, in Fenton's method, stabilisation power of Fenton's reagent and degradation and mineralization capability of photocatalysis are used in removing PhACs. Effectiveness of ozonation in handling effluents of waste treatment plants containing bio-refractory and/or toxic organic pollutants including PhACs has been very well established in some studies [4, 46]. Fenton's treatment improves biodegradability of pharmaceutical wastewater very substantially. Often BOD/COD ratio is increased by 3-5 times making removal of the wastes in the subsequent downstream biological treatment easy. The general observation is that Fenton's process alone can reduce COD of wastewater by around 50% and only when it is coupled with downstream processes like aerobic biological degradation; the COD removal efficiency can go up to 98%. Therefore, total cost of treatment may go up. Ultraviolet–hydrogen peroxide (UV/H_2O_2) combination has also been used to oxidize bio-degradation resistant elusive contaminants in secondary effluents. Fenton and photo-assisted Fenton's oxidation have been proved to be effective in degrading the pharmaceutical residues from laboratory wastes. Fenton's treatment is found to not only stabilize organic matter including PhACs but also facilitate their subsequent removal through oxidation and coagulation.

Photo catalytic activity of TiO_2 nanofibers not only degrade persistent residues like carbamazepine but also enhance dewatering. Individual processes like UV/H_2O_2 process has been found to remove even 90% of selected pharmaceuticals including Carbamazepine at UV dose of 923 mJ cm^{-2}.

Though in some cases almost 100% removal has been reported for some selected compounds using advanced oxidation or irradiation techniques or by a combination of any two, in most of the reported studies, removal of such selected compounds in synthetic wastewater has been done under ideal conditions. In general, irradiation or AOP alone are not found to be so effective and often many intermediates are formed during such processes which even may be more harmful to the ecology than the original contaminants. Dose of radiation is very important and combination of the techniques must be very judicious with total facility for analysis of the intermediates. But it is very important to understand that despite all the drafted success of the AOPs, most of them are limited to being used as pre-treatment options only and they are not established as effective techniques for waste volume minimization with complete removal of the hazards associated with the pharmaceutical compounds[1-2, 47-48].

1.4.4 Adsorption process

Adsorption serves as a useful technique to preferentially remove persistent PhACs. Adsorbents can be used to remove selected obnoxious compounds from treated pharmaceutical wastewater. Thereafter the wastewater is suitable for discharge in the streams. Simplicity of fabrication and environment friendless of adsorbents derived from plant based sources have been demonstrated [49]. However, some pertinent questions remain

regarding the justification in burning tree trunks for the purpose of generating adsorbents for treating large volumes of wastewater generated by the pharmaceutical industries. Majority of the successful demonstrations are in batch mode. In large scale continuous industrial operations, frequent regeneration or replacement of the exhausted adsorbents add to the cost of treatment. For adsorption process to be successful, composition of the waste needs to be explicitly known because Pharmaceuticals and Personal Care Products (PPCP's) bear widely varying adsorption potentials, strongly affected by interactions of complex functional groups and pH–dependence [50].

Recent years have witnessed a spurt in research activities which focussed on incorporation of zeolites for removal of selected compounds and micro-pollutants that are poorly removed by conventional activated carbon based adsorbents [51]. Thus compounds like Metformine and Lincomycine which are fairly common drugs, have been very effectively removed using zeolites. Such success opens up new possibilities of developing methods exploiting the very crystal structure of the zeolites. The compounds with properties like Stokes diameter congruent with that of the silica-alumina lattice of the zeolite can be very successfully removed. Incorporation of magnetic particles and nanotechnology in adsorption has also received increased attention in the recent years. Nanoparticles, nanotubes and allied components as adsorbents hugely increase available surface area, tensile strength and resistance of the material enhancing efficiency of adsorption and in many cases. These materials also counter pH sensitivity, high chemical leaching tendency and other impediments. The high surface area offered by nanoclays (Organically modified layered-silicates) and nano scale particles make them potent adsorbents of pharmaceuticals [52]. Already, carbon nanotubes are established as superior to common adsorbents for removing pharmaceutical compounds like,1,2-dichlorobenzene, trihalomethanes and microcystines[53]. The magnetic particles are capable of adsorbing compounds from aqueous and gaseous systems [54]. When these are combined with nanocomposite materials the resulting magnetic nanocomposite adsorbents are characterized by high selectivity and biocompatibility. But these findings are substantiated by very few researchers on pharmaceutical wastes. So, while we have proof that nanocomposite materials are effective against hazardous heavy metals like lead, chromium [55], their pharmaceutical compound removal indices needs to be explored in details. Thus zeolite based and nanocomposite based adsorbents can be potential new generation adsorbent materials for removal of toxic contaminants from pharmaceutical wastewater albeit necessity for replacement or regeneration of adsorbent material in continuous operation will remain. For treating small volumes of wastewater, adsorption can outperform many other conventional techniques, but treating large volumes of wastewater in continuous plant by adsorption does not appear to be very attractive option. Disposal of the spent adsorbent laden with toxic contaminants will pose another problem.

1.4.5 Coagulation and precipitation

Coagulation and precipitation process serves as an effective pre-treatment step in increasing biodegradability of wastewater through removal of oil and grease, suspended particulate matter, as well as specific compounds. Coagulation is a unit operation that removes colloids from water and wastewater. Its principal mode of action is destabilizing colloidal particles by charge neutralization and promoting collisions between neutralized particles, resulting in cohesion. Usage of the coagulants decreases COD loading at a relatively low cost and also stabilises some of the leaching prone components. Comparative analysis of the commonly available coagulants like lime, alum, ferrous sulphate and ferric chloride have shown that ferric chloride removes BOD_5 and COD to the highest extent. Ferric chloride produces compact sludge with a good settle-ability as reflected in its low sludge volume index (SVI) of 76.3 ± 28.8 ml/g TSS. However, in integrated coagulation–dissolved air flotation (C/DAF) experiments, alum demonstrated higher COD removal (77.5 ± 3.2%) as compared to ferric chloride (71.6 ± 2.9%) and ferrous sulphate (67.7 ± 3.7%). But the removal efficiencies of all the coagulants mentioned above are sensitive to pH changes in the medium while the effectiveness is largely subject to the specific compounds present. For instance, Cheng et.al [56] obtained a poor COD removal rate of 17.2% using polyaluminum chloride at dosage of 0.5 g/ on concentrated effluents from a traizine manufacturing facility. The demerits as well as special features for some of the treatment processes are presented in Table 3. Coagulation-precipitation can only be adopted in reducing load to the downstream secondary treatment unit only.

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September 2017

1.4.6 Electro-coagulation

Electro-coagulation speeds up the conventional coagulation process by addition of electric current and is characterized by formation of hydroxide ions which provides a large surface area for adsorption of organic ions and colloidal particles from substrate; with subsequent separation of the insoluble flocks by electro-floatation. Processes involving electro-coagulation to treat pharmaceutical wastewater has become a popular choice due to improvements wherein alternative energy sources are harnessed to drive the processes. In electro-coagulation, the anode dissolves due to application of electric potential yielding active coagulant precursors. Deshpande et al. [57] applied electrocoagulation to real pharmaceutical wastewater where it significantly decreased the COD loadings by 72% as well improved the BOD/COD ratio from 0.18 to 0.3. They illustrated the energy saving nature, high output in a comparatively small time interval and overall biodegradability enhancement of the wastewater [58]. I Comparison of the COD removal efficiency of electrocoagulation with hybrid associates show that removal power increases progressively in the order: peroxi-electrocoagulation > peroxi-photoelectrocoagulation >photoelectrocoagulation > electrocoagulation [59].This also leads to progressive increase in the costs (especially in Fenton's process where hydrogen peroxide being costly concentration significantly contributes towards overall cost) to attain higher percentage of COD removal. Initial pH of the medium plays a crucial role in governing the overall process performance because it affects the conversion of cations to higher oxidation states, surface charge of coagulating species and COD removal efficiency (which peaks only at an optimum pH level depending upon whether it is following the adsorption or precipitation mechanism). Thus pH needs careful monitoring. The usage of batch systems leaves room for further development and experimentation in continuous mode before this technology becomes robust. A hindrance encountered is the number of reactions which needs to occur simultaneously and optimally; making the process control complex. Improved performances of integrated processes like electrocoagulation and TiO_2 photo-assisted treatment [60] or biodegradability enhancement oxidised by-products on addition of electrocoagulation as a pre-treatment [61] indicates that this technique points to the scope for efficiency improvement. The possibility of flocks and coagulated species turning out to be recalcitrant, increasing eco-toxicity or their power to stabilise and prevent the leaching of the hazardous components needs to be explicitly addressed before the high electricity and electrode costs that currently accompany the process can be justified. Electrocoagulation is thus a process of fast coagulation with the aid of electricity. This is again a pre-treatment process only. The process is sensitive to pH and control of simultaneously occurring reactions is quite difficult. A robust system is yet to be developed for large scale successful demonstration.

1.4.7 Biological treatments

A major section of researches have focussed on using microbes to breakdown the pharmaceutical wastes and to convert them to either harmless or useful forms. The suggested pathways include composting, vermicomposting, anaerobic and aerobic methods [62,63], and their combination some of which yielded valuable by-products [64-65].The very high COD loadings of pharmaceutical wastewater makes it ideally suited for anaerobic processes. Studies have shown biodergability potential of antibiotics in an up-flow anaerobic stage reactor UASR [66] which resulted in a COD reduction by 70 to 75% on antibiotic bearing residues. Some studies [67] report that when a hybrid process combining the anaerobic sludge blanket and a filter in a hybrid up flow anaerobic sludge blanket reactor is applied to treat wastewater, it leads to a very high OLR (Organic Loading Rate) of 8 kg COD/m^3 d together with a fairly high COD removal efficiency of 72% [67]. The biological treatments if critically reviewed would indicate that besides the myriad applications of the aerobic and anaerobic methods in reactor form there are two main applications constructed wastelands and activated sludge and analogous processes, wherein the main concepts with the distinctive characteristics are utilized in effective disposal. A typical biological treatment scheme is exhibited in **Figure 1.**

1.4.8 CONSTRUCTED WASTELANDS

The main hindrance in isolating and individually processing pharmaceuticals is that they are mixed thoroughly with other sewages and this cumulative waste stream enters the municipal waste sewers. Biological processes like activated sludge processes or constructed wastelands can be used to deal with such composite waste mixtures. Pharmaceuticals present in domestic wastewater have been separated in an activated sludge

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September 2017

arrangement followed by their individual processing in a horizontal subsurface flow bed to analyse the removal efficacy of the constructed wasteland of the specific recovered PhACs (Pharmaceutical Active Compounds)[68]. The constructed wetlands used for the removal of pharmaceuticals from wastewater can be classified into surface free water constructed wetlands (SF-CWs), horizontal subsurface flow constructed wetlands (HSSF-CWs), vertical subsurface flow constructed wetlands (VSSFCWs) and hybrid constructed wetlands (hybrid CWs). The constructed wetland H-SSF (Horizontal Sub Surface Flow System) exhibits removal of all therapeutic classes (from 1% for psychiatric drugs to 26% for antihypertensive, on average 16%, with an SD of 8) in the pilot plant setup when it is planted with *Phragmites australis*. The dimensions of the pilot plant are approximately (L × W: 28 m × 1 m, aspect ratio L/W = 28) with depth ranging from 0.7 m at the influent to 1.75 m at the effluent, for achieving the reported removal efficiencies. The main problem in implementation is the requirement of vast swathes of land which might be very difficult to arrange in overpopulated developing countries that are crunched for space. When this method is used for tertiary treatment, escalated costs and complexity both become veritable challenges. Furthermore, the hydraulic retention time (HRT) is about 1 day at a constant influent flow of 8 m^3/day (assuming a water human daily consumption of 150 L/ (day inh). This introduces time constraints which might render it unsuitable when implemented to deal large volumes of municipal wastewater generated by different areas. These two drawbacks are a major handicap for all allied biological processes like lagoons or facultative ponds [69, 70]. Requirement of long residence time and huge space stand in the way of large scale implementation of constructed wastelands.

1.4.9 Activated sludge and allied processes

Usage of activated sludge and analogous processes always make use of similar structures in design when the final effluent quality can be improved if subjected to tertiary treatment such as activated carbon adsorption, additional nutrient removal etc. Overall the activated sludge shows considerable removal efficiencies against selected pharmaceuticals like 68% for tetracycline, 78% for chlortetracycline and 67% doxycycline [71, 72]. But it has to be effective against at least one particular class of drugs to merit economically viable real life implementation especially because most of the unused medicines dumped to the garbage enters the sewers unmetabolized thereby posing a direct risk to the environment [73]. Another potential problem associated with activated sludge process is the presence of biotransformation residues in the output which necessitates further treatment. Though this biological treatment process is considered very successful in large number of industrial wastewater treatment applications, its effectiveness gets little bit diluted in presence of tough PhACs in pharmaceutical wastewater. Around 70% removal efficiency cannot be considered very attractive. Moreover, additional treatment requirement for biotransformation residues adds to the cost of treatment.

1.4.9 Vermicomposting

One of the most promising techniques for solid waste management today is vermicomposting which offers a host of benefits like degradation of chemical compounds, conversion of organic part of the wastes into bio-fertilizer, increasing soil aeration. In one such study [74], the researchers used vermicomposting technique to treat herbal pharmaceutical residues. They treated herbal pharmaceutical industrial waste spiked with cow dung in different amounts using composting earthworm *E. foetida* under simulated conditions in a laboratory environment. Their findings showed considerable changes in chemical characteristics of waste mixtures during vermicomposting with a reduction in pH value of all final residual mixtures. The end product after vermicomposting was more stabilized, odour-free with high range of plant usable forms of soil nutrients with reduction in pH value of all waste mixtures. But these studies used herbal waste residues of plant derived medicines as substrates. So, their applicability in industries against organic and inorganic chemical compounds involved in the production of the vast multitude of medicines in different parts of the world remains questionable. Though vermicomposting has been very successful in solid waste management its role remains confined largely in treating easily biodegradable organic wastes. The myriads of organic and inorganic compounds that may be present in pharmaceutical wastewater cannot be taken care of by vermicomposting approach.

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September 2017

1.4.10 Aerobic and anaerobic digestion

Aerobic and Anaerobic Digestion as well as anaerobic co-digestion (AcoD) of the pharmaceutical concentrates is an effective disposal technique. Using AcoD results in a higher degree of degradation of organics compared to using Anaerobic Digestion on separate substrates [75]. AcoD is an economically viable and environmentally benign option which makes it an attractive choice. It is due to this, there has been a burgeoning of AcoD facilities treating different kinds of biodegradable wastes around the globe with successful examples in Denmark, Sweden, Germany and Switzerland. But persistence of active pharmaceutical remains of different drugs like atenolol, hydrochlorothiazide and diclofenac in the effluents from a full scale integrated treatment of municipal wastewater and OFMSW(organic fraction of municipal solid waste) poses serious questions on the success of the AcoD method when used alone[76]. This approach is yet to be demonstrated in industrial scale for complete removal of PhACs.

1.4.11 Bio-augmentation

An effective way to combat the effects of the pharmaceutical residues present is to isolate the particular elements then use bacterial treatment directly on them to degrade them or convert them into a benign form [77]. This forms the main core of bio-augmentation process that involves usage of microorganisms to remove contaminants from any waste product or a mixture of contaminated sample. They can also be incorporated to increase functioning of activated sludge systems by promoting flocculation and settling of the activated sludge.

An important aspect that is often ignored in the case of the conventional biological treatment methods like trickling filter or activated filter is a prerequisite of a significantly high concentration of carbon substrates (approximately, higher than 60 mg/l of BOD) [78] to maintain a constant concentration of active biomass in the reactor and also during the design stage of recycling biomass from the final products. Bioaugmentation overcomes the problem of continuous supply of inorganic carbon sources. It is also possible to integrate the benefits offered by different reactors like fluidised bed with the aforesaid scheme. The process produces valuable biogas as by-product that makes it more lucrative.

The design of the equipment used for bio-augmentation varies widely. The recent successful experiments used a separate reactor called “Enricher Reactor” where the suspended microbe culture needed for the process were grown and subsequently transferred to the “main reactor”. Saravanane et al.’s research [79] on bio-augmentation using real pharmaceutical industry effluent from Southern Pharmaceutical Industries, Chennai, India delivered some encouraging results. They applied bio-augmentation process in continuous mode to remove an Antibiotic (cephalexin) from industrial effluent that was characterized by high COD loading (12,000-15,000 mg/l,) organic solvents and refractory substances hindering conventional mode of treatment. They attained a maximum COD removal efficiency of 88.5% in continuous mode and at the same time effectively disposed the industrial waste. The main attraction of bio-augmentation approach stems from the possibility of production of biogas and possibility of operation in fluidized bed condition. The technology is emerging as a techno-economically viable option though substantial pilot scale study is still required for full scale implementation.

1.4.12 Biotransformation

Biotransformation is chemical modification of a compound by an organism. It includes use of live organisms often microorganisms to carry out a chemical reaction that is costly or not feasible non-biologically. One of the advantages of using biotransformation lies in its power for retroactive treatments of soils contaminated with pharmaceutical residues as well as in dealing with oestrogens by converting them into readily degradable compounds [80]. Biotransformation with specialized microorganisms develops biofilms that are durable and possess a diverse array of structural and metabolic characteristics which actively helps to remove persistent pharmaceuticals, personal care products, heavy metal traces and toxic minerals. A potential usage of biotransformation is that it can be used as an integrated process to convert APIs such as, atenolol, bezafibrate, ketoprofen, metoprolol, ranitidine, and venlafaxine and other biological process wastes from activated sludge [81].

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Volume 4, Issue 9
September 2017

However, biological methods involve live microbes that are extremely sensitive to changes in pH, temperature, rotational velocity, oxygen levels, substrate concentration as well sudden change in the toxicity levels of the feed. For removing COD from pharmaceutical wastewater maintaining a critical temperature is also essential as the COD removal efficiency is optimum only for a narrow temperature range, a small fluctuation leading to wide variations in separation. Pharmaceutical wastewater when used as a substrate for an aerobic process shows optimum COD removal efficiency when the reactors are operated at a temperature of 30 degree[82] with complete shutdown of biological treatment beyond 60 degree. These factors need to be optimised and controlled carefully because the rate of biological reaction is directly dependent on them. This is a highly specialized plant operation that needs very close monitoring of the operating conditions as well as the biotransformation products using selected microorganisms. Controlled microbial conversions can lead to very successful treatment of pharmaceutical compounds but uncontrolled reaction environment may lead to formation of even more harmful species. Scale up confidence is extremely limited in absence of pilot scale study. In general biological treatment is considered low cost. Among the biological treatment processes, trickling filter and lagoon treatments are the least cost and least efficient types. Activated sludge is moderately efficient and involves cost higher than the lagoons or trickling filters. Though there are a number of comparative studies of different biological treatment practices of actual treatment plants in terms of efficiency, the cost comparisons are only qualitative.

1.5 Advanced processes

1.5.1 Membrane separation

Emerging membrane-based schemes can be very compact, eco-friendly, small, flexible, economically viable, easy to install, operate and maintain as evident in detailed studies [83-91]. Such plants are known for high degree of separation by virtue of high selectivity of the applied membranes but concentration polarization and membrane fouling may stand in the way of sustainable operation unless operated with appropriate module. In quite a few such studies, reusability of the water recovered after membrane based filtration has been demonstrated. In a novel approach of Bloetscher et al., 2012[92], it is observed that integration of a third stage reverse osmosis unit with two stage nanofiltration units can culminate in development of LEED certified water treatment plant. In the light of the above research facilities usage of membrane technology to process pharmaceutical wastewater directly has shown tangible proof of its success and multifarious benefits. Membrane processes with their high separation potential can serve as an effective tool to separate the organic loading along with all the obnoxiously persistent compounds. The modular design, relatively low maintenance costs, high flux and above all the environment friendless makes them a suitable candidate technology. Processes like Ultrafiltration (UF), Nanofiltration (NF) as a possible secondary method to deal with the residues of the medicinal drugs present in municipal sludge of industrial effluents is a viable option. The relative characteristics of different membrane processes are given by **Table 4.**

The treatment of waste concentrates from pressure-driven membrane processes in general and Reverse Osmosis (RO) process in particular has been studied in some details. There are quite a few researches conducted in this field which have developed techniques to treat secondary RO concentrates. In a recent study [93], it is observed that nanofiltration-forward osmosis integrated system can be very effective in treating complex and hazardous pharmaceutical wastewater. This study presents a remarkably novel approach in pharmaceutical waste treatment as it leads to new policy suggestions in industrial wastewater treatment particularly in the context of the hugely populated growing economies of the world. However, commercialization demands that such plants should be not only efficient but economically viable also. Thus the studies of Pal et al.[94-95] that present such development of operational strategy along with techno-economic analysis need to be considered. Processes used to treat primary as well as secondary RO effluents have been studied extensively and the relative merits and demerits of different classes of treatment have been summarised.

Emerging technologies like Forward osmosis (FO), Membrane Distillation (MD) have been harnessed to decrease waste volume generated by RO process, recover water and other components from the RO

concentrates. In such hybrid processes, energy required is also considerably less. However, there is no mention of the fate of the final concentrated effluents from the FO processes which is quite important because treatment alone will not suffice as an effective waste management strategy. The danger of eco-toxicity posed by the active pharmaceutical compounds still persists; so does the risk of reaction of these compounds with other agents when they are disposed in the landfills. However, the issue of effective management and disposal of the solid residues can be done through stabilization of the sludge followed by drying and disposing. If the final disposal can be done effectively, membrane based treatment technologies have all the potential to emerge as the most sustainable technologies. So far separation and purification is concerned, the tailor-made membrane by virtue of high selectivity can ensure complete separation of the toxic contaminants from water which no other conventional and even emerging technologies can at the moment promise without additional adverse impact on the environment.

1.5.2 Irradiation process

Many pharmaceutically active compounds (PhACs) such as antibiotics, hormones and X-ray contrast agents, antineoplastic drugs and anti-inflammatory drugs can be successfully removed using gamma ray irradiation technique or ionizing irradiation. The major advantage ionizing irradiation is the high efficiency of removal reaching almost 100 per cent. However, in application of irradiation technique, utmost care needs to be taken in applying effective radiation dose. At low doses (viz., 0.1-0.4 kGy), often large number of intermediate by-products are formed where detection and even their analysis turns very tough and many such intermediates are even more harmful than the originally existent PhACs. Radiation dose above1kGy needs to be employed for complete degradation without leaving the potential risk of generating more harmful intermediates. Combined treatment using H_2O_2 or TiO_2 along with gamma irradiation can be more effective [**96].** That irradiation techniques can remove pharmaceutical ingredients from various pharmaceutical waste streams with high degree of efficiency at high radiation dose has been described in very detail in study [96]. However, no comprehensive treatment scheme based on irradiation technique has come up with scale up confidence.

1.5.3. Hybrid process

Membrane-integrated Hybrid Technology

Membrane bioreactor is a powerful equipment to treat consolidated form of pharmaceutical wastewater and municipal sludge. It offers a host of advantages like higher efficiency than conventional processes, better sludge retention, greater compactness, capability of withstanding fluctuating pollution loads while maintaining reasonably consistent quality of the treated water. Pilot plant scale study has demonstrated COD removal efficiency of membrane bioreactor to be greater than 95% [97-98]. This makes it a particularly lucrative option for treating medicinal wastes that are characterized by very high COD loadings. Owing to the effectiveness of the additives and the specific treatments like electrocoagulation, advanced oxidation process etc. against a particular class of pharmaceuticals, the schemes where membrane bioreactors are integrated with some conventional techniques have been considerably successful. An entire segment of researches are directed towards membrane bioreactors encompassing possible integrations with other existing processes or new schemes like a fungal bioreactor, submerged membrane electro-bioreactor (SMEBR). A typical membrane-bioreactor is exhibited in **Figure 2** whereas a more compact design is presented in **Figure 3.** Innovative combinations of integrated membrane bioreactors and TiO_2 photocatalysis process for the removal of non-degradable drugs such as carbamazepine from simulated pharmaceutical industrial effluent has been carried out. The research reveals that if a recycling ratio of 4:1 is adopted it will yield a removal rate of 95% for carbamazepine. Besides the reduction of effluent chemical oxygen demand (COD) and increase in sludge yield, respirometric tests suggested that the oxidation products are mostly biodegradable and they do not affect microbial activity adversely. In some studies, the conventional physical processes like adsorption are integrated with the bioreactors either by selectively removing some adsorbents and then transferring the bulk to the bioreactors or by segmenting and treating the inorganic constituents in the adsorption chamber and inorganic parts in the reactor chamber. Though quite a few of them scores highly on the innovativeness quotient, their effectiveness in large scale, continuous, real life situations remains to be assessed [99-102]. Some membrane-integrated hybrid treatment schemes are shown in **Figure 4 and Figure 5**.

A membrane-integrated hybrid treatment has the potential of not only turning hazardous wastewater reusable but can also significantly add economy to the plant by helping to recover valuable byproducts. A classic example is recovery of struvite from hazardous wastewater using Fenton's method integrated with downstream membrane separation [103]. This study [103] presents a very novel approach in hazardous wastewater treatment indicating that judicious selection and logical sequencing of unit operations during wastewater treatment can turn non-revenue wastewater treatment plants economically attractive.

1.5.4 Membrane-integrated thermophilic process

Thermophilic processes (TPPs) are characterized by high removal yields of organic matter [105], and are ideally suited for treatment of wastewaters bearing hazardous compounds or having a high salinity gradient [107]. Thermophilic treatments show high removal kinetics of biodegradable substrates which is about 3 to 10 times higher than those measured in mesophilic conditions [105]. Integrating thermophilic processes with a membrane reactor eliminates the disadvantage of poor sludge sedimentation that results from the inability of forming flocks by the concerned particles in suspension. For dealing with high strength liquid residues (rich in organic matter-Chemical Oxygen Demand (COD), nutrients and salinity) directly from a pharmaceutical industry Thermophilic Aerobic Membrane Reactor (TAMR) allows processes to operate with higher concentration of biomass (higher than 50 kg TSS m^{-3}), resulting in a drastic reduction of the reactor and aeration tank volumes. Thermophilic membrane bioreactors represent a very compact system but suffer from some drawbacks such as a very low sludge production rate and the necessity of biomass acclimatization which needs to be addressed before it is projected as a competitive process.

In the field of separation and purification, membranes can do wonder in terms of degree of purification. Membranes can be tailor-made and can be fabricated today with versatile compatible materials promising high selectivity, reasonably high flux and durability. The problem of membrane fouling being the major hindrance in successful employment of membranes in purification job has been largely overcome through better design of fouling-free membrane modules. However, to avoid requirement of frequent cleaning of membrane or its replacement, finest separation job must always precede pre-filtration steps using microfiltration or ultrafiltration. Integration of conventional coagulation-precipitation can hugely reduce the filtration load of the fouling-sensitive membranes. With progress of time emergence of new generation membranes with remarkable characteristics in terms of selectivity, flux, durability, fouling resistance, temperature resistance and even resistance against large varieties of chemical solvents coupled with development of fouling-free modules has opened up the avenues of development of membrane-integrated hybrid technologies which are inherently sustainable.

However, scale up confidence has not yet reached the stage for immediate transfer of membrane-integrated hybrid technologies to the field for commissioning. This calls for extensive pilot scale studies along with techno-economic analysis that will eventually pave the way for scale up of the sustainable technology for deployment to ensure protection of the integrity of the surface water resources.

1.6 Sludge disposal techniques

1.6.1. Sludge stabilisation

Every treatment scheme is bound to land up with the problem of sludge disposal. Unless this issue is addressed in the scheme of treatment, no waste management scheme can be considered as sustainable. Unlike the sludge generated in conventional chemical-coagulation-precipitation plants, the sludge resulting from pharmaceutical wastewater is predominantly organic thereby turning its stabilization in a solid matrix very difficult. Very limited attempts and that too on a few selected compounds have been made in the context of stabilization of pharmaceutical sludge. Of late, focus has shifted from broad spectrum stabilizers to chelating agents. Chelating compounds like octolig (a polyethylene-diamine covalently attached to high-surface area silica gel) can quantitatively remove anions (nitrate, nitrite, phosphate, sulphate) from aqueous solutions [106]. But, these chelating agents work only on compounds possessing analogous ions. So, while Octolig can completely remove three xanthenylbenzenes (rose bengal, eosin Y, erythrosine) with phenolic and carboxylic acid groups and also can quantitatively remove zinc phthalocyaninetetra sulfonate (ZPS) and lissamine green

B (bearing sulfonate groups); it fails to treat methylene blue and analogous groups with quaternary ammonium compounds [107]. As the binders like cement are primarily suitable against inorganic compounds, the first logical step in stabilization of pharmaceutical sludge is drastic reduction of its organic loading. Another big problem in stabilization study is failure of conventional leaching test (TCLP) in the context of pharmaceutical sludge due to the plurality of diverse chemicals. Detection of leakage of the main hazardous components and thereby determine the effectiveness of the stabilisation is extremely difficult. Despite high success in lab-scale, industrial scale application has not yet been tested with these emerging stabilizing agents. This brings home the point that sludge stabilization issue in the context of pharmaceutical waste handling has not been addressed adequately. Substantial pilot scale studies encompassing techno-economic aspects need to be taken up urgently towards sustainable solution to the environmental problem arising from discharge of pharmaceutical wastewater [108-111].

1.6.2 Disposal: Incineration and landfilling

The common methods adopted for disposal are incineration, open burning and landfilling. The group of processes that use incineration can be segregated as warm disposal technologies and high-temperature thermal disposal technologies. Such incineration may be with measures for air pollution control or without such measures. Often simple incineration involves open air burning without adopting any ash disposal practises or measures to curb any possible spread of disease causing germs. The diverse categories of pharmaceutical wastes are often combined prior to incineration or other disposal options. That such an approach may be quite dangerous from environmental point of view and necessary separate incineration facilities should be in place is evident from some studies [112-113]. Landfilling has often been adopted as an option for medical waste disposal. But landfilling option is neither a full proof one in arresting the contamination of water bodies with the leachates nor such a technique can effectively neutralize the toxic effects of the hazardous compounds and the chain reactions they undergo in presence other wastes. The endocrine disrupting nature and the power of bioaccumulation make pharmaceutical residues in the leachate leakages from the landfills dangerous. The good removal rates obtained across different wastewater plants does not necessarily tantamount towards effective degradation of pharmaceutical compounds. Thus the studies [114,115] assume significance in pointing out the pitfalls of using ordinary landfills to handle hazardous wastes. There are even important studies[116] that have modelled simulation of waste-behaviour in landfills and used models such as LandSim (Landfill Performance Simulation) modelling program for analysing the environmental consequences of leachate release from a MSW (Municipal solid waste) landfill bearing household hazardous waste (HHW). In some cases, sanitary landfills replacing ordinary landfills offer some safeguard against the potential threats but they are insufficient to effectively combat the huge volume of the medicinal waste worldwide [117-118].

Incineration cannot be considered environment friendly as it only shifts the pollutants from water to air in a different form and transfers pollution from a local area to a global one. The major objection against thermal incineration is release of dioxin to the atmosphere during incineration. After the SARS (Severe Acute Respiratory Syndrome) epidemic in 2003 in China, the National authorities in China quickly planned for dedicated centralized medical waste disposal facilities with major emphasis on non-incineration methods. However, in cases of extreme infection potential associated with hazardous medical wastes, this often appears as the only viable option in absence of an eco-friendly option. Thermal incineration processes must be accompanied with downstream air pollution control devices like adsorber, scrubber, electrostatic precipitators so that concentration of dioxin never exceeds 0.1 ngTEQ /Nm^3. Research efforts need to be directed towards evolution of eco-friendly techniques that can eventually replace incineration. So far landfilling is concerned, the practice can hardly be called a scientific approach unless sludge is well stabilized so as to prevent leaching out of harmful components that eventually contaminate both surface as well as groundwater resources. Though bit expensive, only sanitary landfilling should be allowed and that too with prior effective stabilization of the harmful compounds.

1.6.3 Zero discharge approach: green pharmacy and biopharmaceuticals

The best strategy in any waste management approach is invariably the zero discharge approach. The principle is to make the process green so as not to generate any waste. Though practically achieving zero discharge is extremely tough nevertheless the production processes can be made as green as possible leading to

insignificant waste generation. One such approach is called green chemistry approach or green pharmacy approach. In this concept, the entire life cycle of a product is monitored and the product is made as innocuous as possible [119]. The production routes are so chosen that they can be accomplished in relatively few steps, involving less energy, less material, producing minimum undesirable by-products and even making the by-products easily biodegradable. This approach turns the whole production process eco-friendly [120-121].

Another green production approach envisages production of biopharmaceuticals using biotechnology. They also include usage of biocatalysts especially isolated enzymes and microorganisms in the production of pharmacologically valuable materials. They not only ensure environment friendliness but also offer economic advantages over the synthetic catalysts [122]. The most direct impact is expected on pharmaceutical waste management. Many obnoxiously persistent active pharmaceutical compounds that permeates most of the waste treatment plants, can now be developed into potentially biodegradable forms with the help of bio-catalytic processes. Already, there are instances of synthesis of small molecule active pharmaceutical ingredients (APIs) such as simvastatin, atorvastatin, pregabalin, paroxetine and levetiracetam using green pharmacy [123]. Simvastatin can be obtained with high conversion (>99%) and high purity (>98%), while Atorvastatin synthesis with biotransformation is characterized by high throughput (200 g/L-d), high yields (90–95%) and excellent stereo control (98% enantiomeric excess (ee) and 97% diastereomeric excess (de) [124]. One of the major benefits of this technique is that the process steps to atorvastatin are not only truncated but two of the most energy intensive steps could be bypassed saving on energy costs while leading to reduction of waste (implying material saving in terms of solvents and raw materials). Such material saving is estimated at hundreds of metric tons per year. Application of this technique eliminates use of hazardous reactions, as in the case of Levetiracetam when conventional alkylation is replaced by benign S_N^2 reaction using cheap pyrrolidinone. Though there are diverse opinions on biodegradability of biopharmaceuticals, there is no doubt that the manufacturing process involves less energy, less material and generates minimum wastes circumventing the threats of pharmaceutical wastes[125]. Using membranes, wastes can be concentrated to a very high level that facilitates solid disposal with reduced volume. **Figure 6** shows one such scheme. Though green chemistry approach at this stage may not be economically attractive to the pharmaceutical manufacturers, in the long run this will be beneficial to all the stakeholders and the environment. Green production processes need to be investigated on larger scale to raise scale up confidence for commissioning of green plants as fast as possible. A green production process brings about process intensification that not only results in eco-friendly production but also brings lots of operational flexibility involving even less manpower, material, energy and capital with the promise of higher profit margins [121].

1.7. Conclusion

Literature reveals that integrity of the surface water resources is yet to be protected effectively from the onslaught of discharge of hazardous pharmaceutical wastes. Pharmaceutically active compounds pose threat to the ecosystem through their continuous accumulation, their toxic and persistent nature and potential of developing drug-resistant microbial strains. That analysis of treated wastewater in many cases shows presence of pharmaceutically active compounds only indicates failures of the existing treatment technologies. Though thermal incineration of highly hazardous medical wastes has been adopted in majority of the cases, this approach has never been environmentally justified because of release of dioxin and indirect transfer of obnoxious substances from one phase to another phase in the environment. It is extremely difficult to assess presence and eco-toxicological effects of thousands of pharmaceutically active ingredients in water environment. Therefore, it is advisable to focus on the most frequently used and most persistent pharmaceuticals. Extensive research on treatment of pharmaceutical wastes have been conducted over the decades but majority of those concentrated on lab-scale studies with synthetic solutions only raising very little scale up confidence in absence of techno-economic feasibility studies. As the problem persists and rather magnifies with increasing population and increasing production of pharmaceuticals with commensurate discharge of hazardous wastes from the production plants, a paradigm shift in this waste management strategy is necessary. Green chemistry approach in pharmaceutical production and biological transformation of the waste pharmaceutical ingredients into harmless products appears to be the most environmentally desired

option. The best technology selection will depend on long term environmental desirability, efficiency of the technology, social acceptability and economic viability. Research efforts towards development of new treatment schemes will obviously continue. But the present state-of-the-art demands that instead of only venturing into hundreds of treatment options on lab-scale, some of the well identified technologies such as membrane-integrated hybrid technologies having all the promise of high degree of separation-purification at affordable cost needs to be studied urgently on pilot scale encompassing all techno-economic issues. This will at least pave the way for implementation of some sustainable technologies at the earliest till more sustainable technologies evolves. The best strategy will, however, be switching over to green production technologies. Till total switching over to green technology, search should continue to develop innovative technology that will permit sustainable treatment and reuse of reclaimed water.

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Table 1: Typical Charateristics of pharamceutical effluents

Parameters	standard effluent values
BOD	900-400 ppm
COD	2000-6000 ppm
PH	1.5-6.0 (variable)
OIL AND GREASE	35-2000 ppm
TDS	1350-7250 ppm
TSS	500-2000 ppm
TKN	800-1000 ppm

Table 2: Sources of Pharmaceutical wastewater contaminants

Process liquors	Organic synthesis	Contaminated solvents
Spent fermentation broth	Fermentation processes	Contaminated waters
Spent natural product, raw Materials	Natural product, extraction processes	Leaves, tissues
Spent aqueous solutions	Solvent extraction processes	Contaminated water
Leftover raw material, Containers	Unloading of materials into process equipment	Bags, drums (fiber, plastic, metal),plastic bottles
Volatile organic compounds	Chemical storage tanks	drums Solvents
Spills	Manufacturing and lab Operations	Miscellaneous chemicals, mercury, other metals

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Wastewater	Equipment cleaning, extraction Residues	Contaminated water, phenol-based
Spent solvents Solvent	extraction or wash practices	Contaminated solvents

Table 3: Features and limitations of different treatment options [132]

Technology	Features	Limitations
Precipitation	Suitable for large scale operations Can treat high salt content waste	Efficiency depends on solid liquid separation step
Sedimentation and settleable solids.	Primary treatment; removes floating Needed.	Large quantity of reagent
Coagulation And Flocculation Purification of treated water.	Can be used for building a compact treatment plant or for further	Preliminary chemical Coagulation and flocculation are generally not used.
Ion Exchange Stability. Ensuring high selectivity	Good chemical, thermal and radiation	Blockage problems needs regeneration
Evaporation High volume reduction factor Suitable for a variety of radionuclides	Well established technology	Process limitations include foaming, corrosion High capital costs
Solvent Extraction	Selectivity enables removal and recycling of actinides.	Generates aqueous and organic secondary waste

Table 4: Qualitative comparison of different membranes. [133]

Process	Membrane	Transfer Mode	Pressure (atm)	Flux (L/m^2h)
Microfiltration	Porous Isotropic.	Sieving and Adsorption	500-10,000	0.5-5
Ultrafiltration	Porous Asymmetric	Sieving and preferential	100-2,000	1-10
Nanofiltration	Finely porous Asymmetric or Composite	Sieving or electrostatic hydration or diffusive	20-200	7-30
Reverse Osmosis	Nonporous Asymmetric Or composite	Diffusive	10-100	20-100

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FIGURE NO. CAPTION

Figure 1 A typical biological treatment scheme

Figure 2 Bioreactor treatment scheme

Figure 3 A compact membrane bioreactor module

Figure 4 A Membrane- integrated Hybrid Treatment scheme

Figure 5 Membrane–integrated Hybrid Treatment schemes: (a) using bonding coupled with membrane filtration (b) using floatation integrated with submerged membrane filtration.

Figure 6 Treatment of concentrates from a membrane process

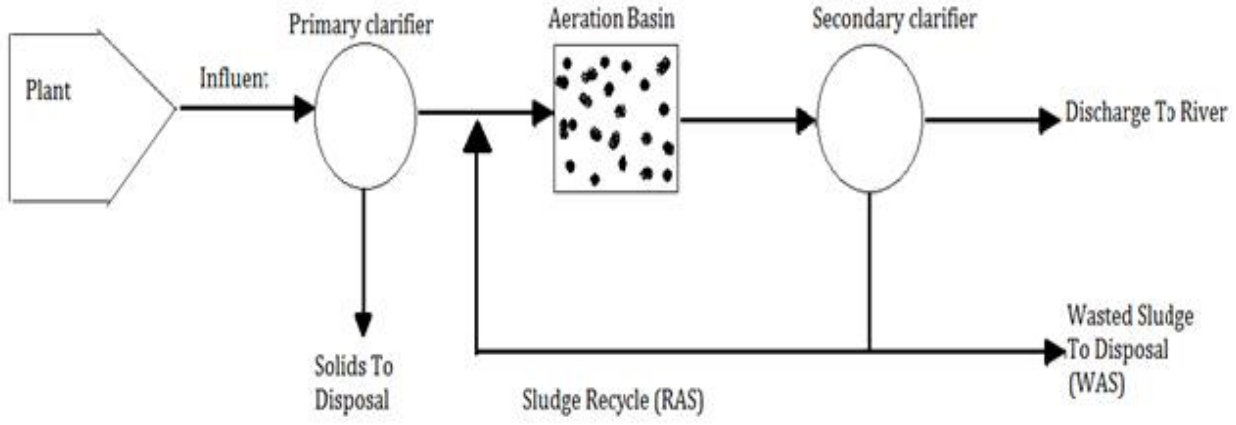

Figure 1: A typical biological treatment scheme

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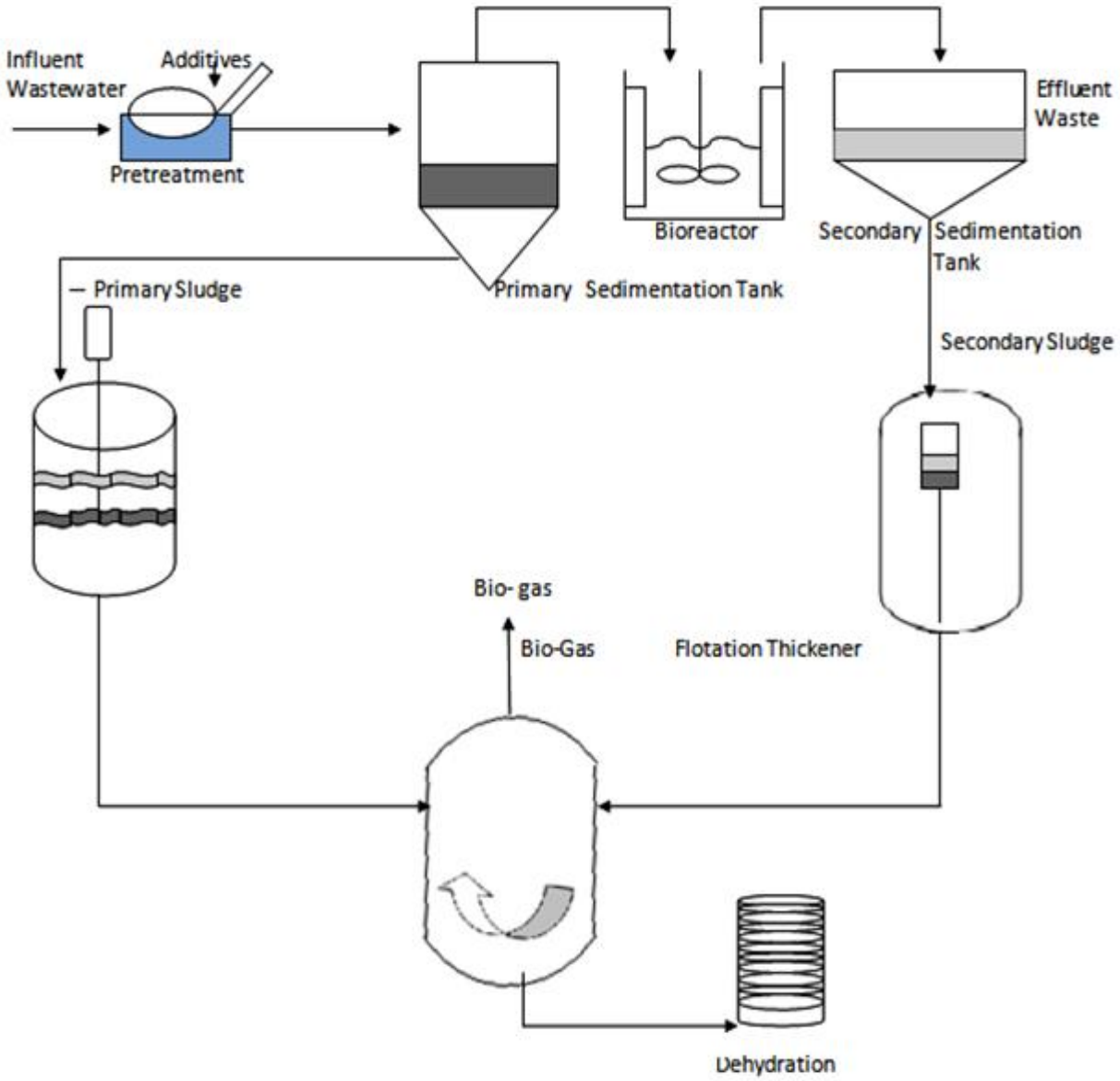

Figure 2: Bioreactor treatment scheme

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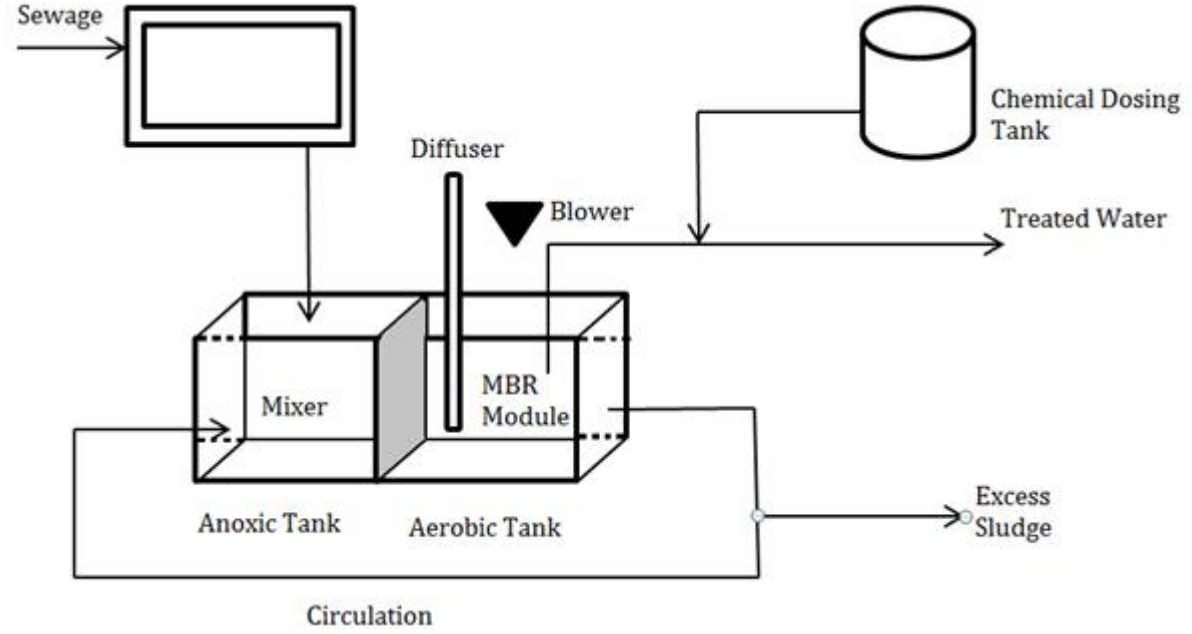

Figure 3: A compact membrane bioreactor module

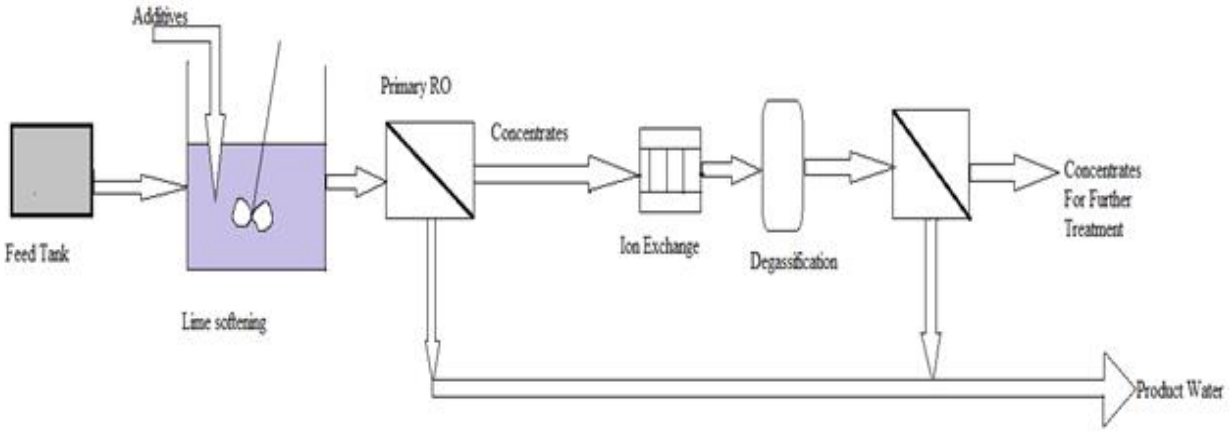

Figure 4: A Membrane-integrated Hybrid Treatment Scheme

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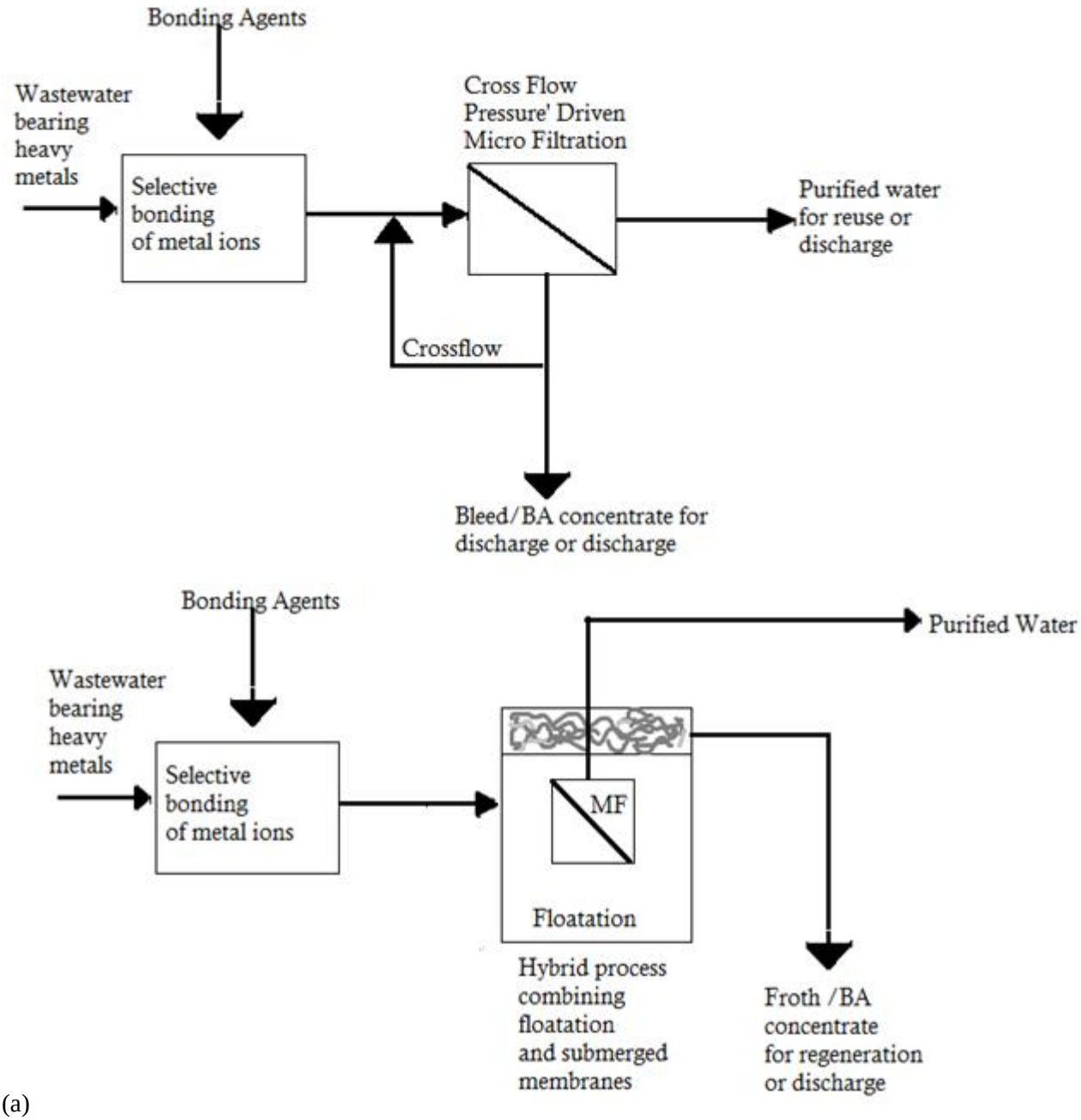

(a)

(b)

Figure 5: Membrane–integrated Hybrid Treatment schemes: (a) using bonding coupled with membrane filtration (b) using floatation integrated with submerged membrane filtration.

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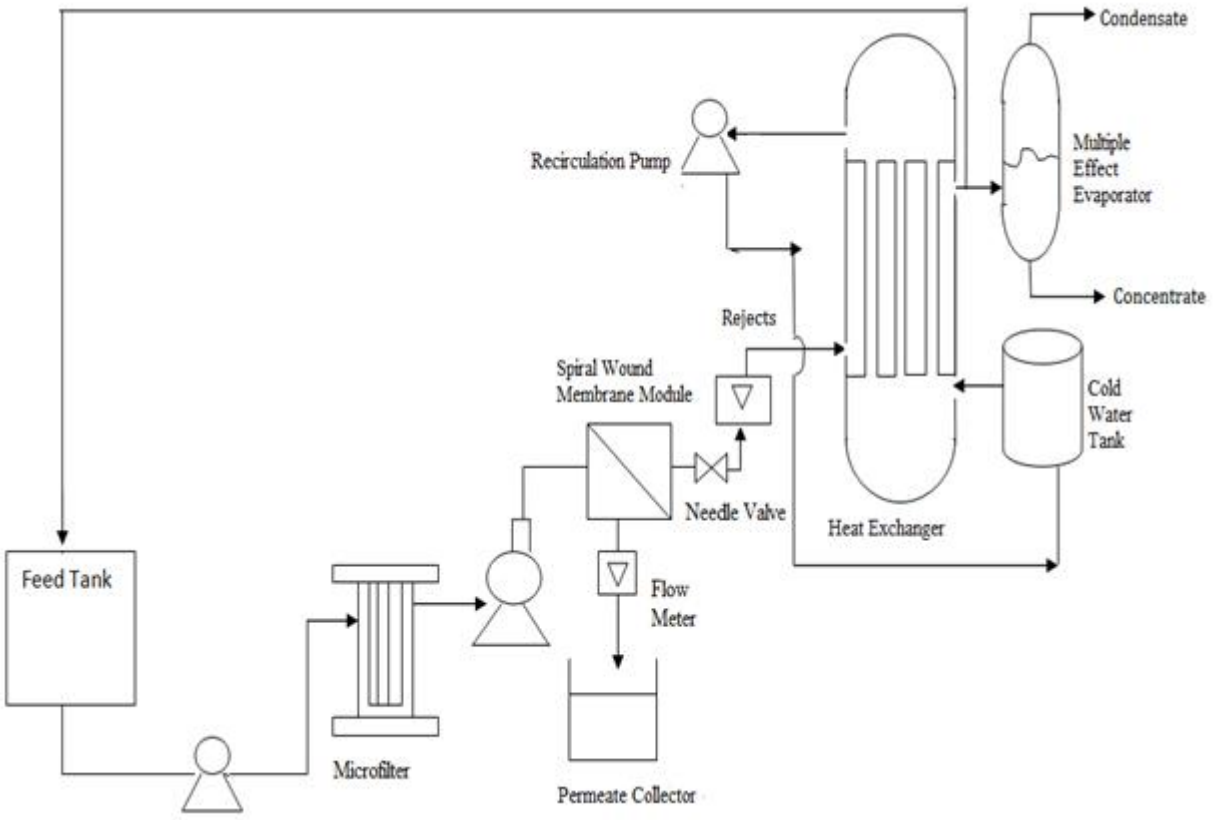

Figure 6: Treatment of concentrates from a membrane process [107]