Application of Pharmaceutical Engineering: A Useful Technological Protocol in Pollution Control of Toxic Pollutants in Pharmaceutical Industry

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Abstract:

There exists a common idea that toxic chemicals are generally produced by chemical industries. While pharmaceutical industries are the only producers of antidotes and medicines to cure ailment of the patient. The pharmaceutical industries have shown a rapid growth in last few decades with the advent of latest G.M.P. and automation, but advancement in the field of pollution control in pharmaceutical plants still found to be sluggish, particularly in developing countries. This article will provide information to technical personnel of pharmaceutical industries regarding different toxic pollutants generated during the operation of pharmaceutical plants and their control based on commercial feasibility. Different ways of pollution control like waste minimization from the source, recycling and reuse, control of dusts and toxic volatile gases from boiler and production plants by filter and adsorbents , use of aqueous coating technology for reduction of chlorinated hydrocarbon in air, control of spilled materials in storage and processing areas have been discussed. Various technologies and devices have been mentioned for pollution control of waste water like Bar Screen, Flocculation, Sedimentation, Gravity Coagulation, Adsorptive Bubble separation, Activated Sludge Process, Trickling Filter, Aerated Lagoons, Reverse Osmosis, Ultra Filtration, Ion Exchange Resin, and Membrane Filtration. After treatment water can be reused for pharmaceutical production.

Key words: Toxic pollutants, Pharmaceutical Engineering, Adsorptive Bubble Separation, Waste Management, Pollution Control, Pharmaceutical industry.

INTRODUCTION:

The prime objective of this article is to present a review on different applications of pharmaceutical engineering as guidelines to control pharmaceutical pollutants as well as categorize the different pollutants generated by pharmaceutical

industries. The wastes generated as pollutants by pharmaceutical industries in air and water include a variety of chemicals like powder of different drugs & pharmaceuticals, toxic volatile solvents like ethanol, methanol, methylene chloride, isopropanol, carbon tetrachloride, acetone, benzene, heavy metals, a variety of metallic cyanides which are toxic to human and animal kingdom in lethal and sub lethal doses. This guide line will help prevent to control environmental pollution by process control and process development ,waste minimization technique from the source itself and set up of pollution controlling equipments.The article has also highlighted the economy of the industry by waste minimization along with simultaneous control of environmental pollution. The pharmaceutical industries in third world countries have shown a rapid growth in last few years, but growth in pollution control sector is not up to the mark. Pollution control norm is not stringent in most of the developing countries and pharmaceutical industries in these countries try to find the solution on their own without the consultation of technical experts. This review article may help the professional agencies as well as pollution control authorities[Central & State Pollution Control Boards,State Pollution Control Agencies in India and particularly in Third World Countries. In U.S.A., U.S. Environmental Protection Agency is conducting advanced researches in this field. In our country,Enviro Care System in Chennai, a private professional agencyis also interested in this field.] provide information and guidelines for solutions to combat the pollution related problems. This review work has categorized the different pollutants discharged by different sections of pharmaceutical plants. The article also suggests that pharmaceutical companies should adopt suitable cost effective methods and install proper devices for treatment of waste generated during operation of the plant.[1,2]

1. POLLUTANTS GENERATED BY DIFFERENT SECTIONS OF PHARMACEUTICAL PLANTS:

1.1. Research and development sections: This section is engaged in a variety of research activities like Chemical, Microbiological, Biopharmaceutical and Pharmacological with trained specialist personnel and generates pollutants like Halogenated and Non-halogenated hydrocarbons, Organic solvents, Photographic chemicals, Radio nuclides, Bases and Acids etc. Waste water is categorized by high level of B.O.D, C.O.D, and T. S .S with pH 1-10.[1]

1.2. Chemical synthesis plant: Most drugs are produced by chemical synthesis through a number of unit operations involving organic and inorganic reactants, catalysts and a wide variety of solvents employed for product recovery. Waste water is categorized by high level of B.O.D C.O.D, and T.S.S with PH-1-11.[1]

1.3. Natural product extraction plant: Pharmaceutical products of natural origin are extracted with a variety of solvents from roots,

leaves and animal glands. They are allergy relief medicines, Alkaloids, Insulin, Morphine, papaverine. They are recovered by different organic solvents

Like ketones and alcohols and inorganic salts of zinc and lead. Waste water is characterized by low level of B.O.D, C.O.D, and T.S.S and pH in the neutral range of 6 to 8.[1]

1.4. Fermentation plant: Steroids, B-vitamins and antibiotics are the typical products of fermentation plants. Process includes inoculation, seed preparation, fermentation, product recovery by solvent and purification. The typical waste water is composed of spent fermentation broth, microbial flora, organic solvents, washed water from equipment's cleaning and scrubbed fermenter's vent gas. It has high B.O.D, C.O.D, and T.S.S with pH range of 4-8.[1]

1.5. Formulation plant: This plant generates a variety of dusts and toxic fumes during the production of different dosage forms. Unit operations like shifting, granulation, drying, filling, coating, strip and blister packaging generate toxic dusts of pharmaceuticals and adjuvants. Fumes of isopropyl, ethyl alcohols and acetone are produced during production of tablets. Coating and packaging section generates a variety of toxic fumes like methylene chloride, isopropyl alcohol, carbon tetrachloride and benzene. Polyvinyl chloride and polyvinyl dine chloride are the toxic fumes of blister packaging sections. The typical waste water constitutes inorganic salts, sugars and syrups with low B.O.D, C.O.D, and high T.S.S with near neutral pH of 6-8.[1]

1.6.Steam boilers: Oxides of nitrogen (NO_2 and NO) , sulphar (SO_2 and SO_3) and carbon (CO and CO_2) are the typical air pollutants generated due to natural gas combustion used as fuel for production of steam utilized by different sections of the pharmaceutical plant during operation. These inorganic oxides are highly toxic and these are to be treated prior to discharge in air.[1]

2. METHODS TO CONTROL AIR POLLUTION:

2.1Treatment of Flue Gas for removal of oxides of nitrogen from steam boiler: Flue Gas can be decomposed by catalyst like alkali and alkaline earth metals at higher temperatures in fluidized bed condition to remove oxides of nitrogen.

2.1.1Oxides of nitrogen is reduced to nitrogen by Ammonia in presence of Palladium catalyst by the following reactions:

$$8NH_3 + 6NO_2 = 7N_2 + 12H_20$$

$$4NH_3 + 6NO = 5N_2 + 6H_2O$$

$$4\ NH_3 + 3O_2 = 2N_2 + 6H_2O$$

2.1.2. It can be removed by adsorption using solids like Alumina, Silica Gel, Molecular Sieves and Ion Exchange Resins, adsorption by Sulphuric Acid or alkaline solutions.[1,3]

2.2. Desulfurization of Boiler's Fuel for reduction of Sulphur dioxide from the boiler: (i) Pulverized lime stone is injected into the boiler, it absorbs SO_2 after calcinations. (ii) Injection of

dry lime stone and subsequent removal of calcined lime stone by scrubbing to remove SO_2 from the flue gas.(iii) Alkalized Alumina(Na_2O and Al_2O_3) can be used to remove SO_2 from Flue Gas. [1, 3]

2.3Major methods for removing organic vapors from air : These are Carbon Adsorption, Air Incineration and Liquid Scrubbing.(d) A combination of air adsorbent – air incineration method have been found to be most effective to control pollution due to organic vapor.[3]

2.4. **Methods to maintain healthy, dust free and sterile environment inside the pharmaceutical_manufacturing, storage and quality control areas :**(i) High Efficiency Particulate Air(HEPA) filter of 0.22micron porosity followed by Particulate Matter Retention (PMR) filter of 5-20 micron porosity. Area is maintained air conditioned by central air conditioning system under specified positive pressure differential by Air Handling Unit (AHU) for sterile products.(ii) For areas of non sterile products as well as packaging , Particulate Matter Retention Filter of 20 micron porosity with on line AHU is suggested. Monitoring of particulate count, air flow rate from HEPA, pressure differential by manometer, humidity and temperature of each area are to be the routine measurement to maintain the standard of air.[4]

2.5. **Waste minimization methods from source to control air pollution:**(i) Internal floating roofs should be arranged to control air emissions of hazardous vapor of solvents from bulk storage.(ii) Dedicated dust collectors should be used and reworked dust back into product at the point of tablet compression, capsule filling, powdered injection filling, filling of dry syrups and different unit operations of tablet and capsule manufacturing.(iii) Fossil fuel combustion should be optimized.(iv) Dedicated vent condensers should be used ; arrangement should be made to return the condensate to source.(v) Nitrogen purge rates should be maintained at minimum through vapor space of agitated reactors.(vi)Toxic fumes of chlorinated hydrocarbon like Methylene chloride will be reduced, if aqueous coating of ethyl acetate with 10% methylene chloride is applied to tablet with new spray equipment attached to Auto Cota machine. In this way, air pollution due to chlorinated hydro carbon can be reduced to 90% without using pollution controlling equipments.[1]

3. WASTE MINIMIZATION METHODS TO CONTROL IN PROCESS WASTE:

3.1. Empty containers in waste stream should be returned to supplier. They can be rinsed triple and given to the production line or containers with recyclable liners can be used. They can also be remolded by in house molding machine and given to production line.3.2. Waste from equipment cleaning can be minimized by maximizing the quantity of batch sizes of each product in order to reduce the cleaning frequency and consequent waste generation.

Final rinse can be used as pre-rinse for the charge of the next batch. Wiper blade should be used at

the end of the process and material should be transferred to the product to reduce the waste in water. Spray head cleaners with high efficiency of cleaning using low volume of water
may be suggested to reduce the volume of waste water. 3.3. Waste from spills and area wash down can be controlled by dedicated vacuum system, dry cleaning and usage of recycled water.

3.4. Toxic non aqueous solvent should be replaced by aqueous system,particularly in Tablet Coating Section and their quantity reduced and these are to be recovered after the process.(iv) Validation of cleaning should be done to reuse the production material.[1].

4. WASTE MINIMIZATION METHODS FROM SOURCE TO CONTROL HAZARDOUS WASTE: In a pharmaceutical industry, hazardous wastes are generated by spillage and leakage of hazardous chemicals during storage and handling. These are volatile flammable liquids and explosive dusts. These may create flammable and fire catching vapour and dust explosion. These include volatile liquids like Acetone, Methylene chloride, Methanol, Ethanol, Isopropanol and explosive powder like Sulphur Drugs etc.. Their waste can be controlled from source by the following waste minimization methods:

4.1 Material substitution: It is the process of replacement in one or more of the raw materials used in production to reduce the toxicity of hazardous waste as well as volume of waste generated.

This method can be applied in charging of tablets & capsules by replacing volatile non-aqueous solvent wet granulation by aqueous wet granulation and direct compression .In case of coating technology, non aqueous solvent can be replaced by aqueous solvent. Other methods of material substitution are aqueous based cleaning solutions in place of solvent based cleaning solutions and chlorinated solvents replaced by non- chlorinated solvents.[1]

4.2. Demerits of material substitution: (i) Quality Assurance problem of the modified formulation.

(ii) Considerable time required for approval from the licensing authority of the reformulated drug. The right approach is to develop the formulation from the very beginning by aiming to reduce the toxicity. This is an integral part of Research and Development section.[1]

4.3. Process modification: It reduces By Product formation by controlling reaction parameters, reactor's efficiency. Increased automation will reduce operator errors. Usage of conveyer belts
will help reduce spillage. Proper Agitator design and optimization of operating temperatures will resist unwanted deposits due to crystallization, sedimentation, polymerization and corrosion. In a synthetic drug manufacturing plant, transfer by pump will eliminate material losses.[1]

4.4. Demerits of process modification (i) Process validation is required to ensure the

acceptability of the product. (ii) Approval of licensing authority is required prior to introduction of the new change.

(iii) Good Operating Practices (G.O.P.) is another management technique applied for day to day operation of the plant which includes Plant Management, Materials Handling and Waste Management. Plant Management includes introduction of management incentives given to expert employees who have successfully reduced or recycled waste and increased the yield of production, Employee Training, Additional Documentation in the form of S.O.P with respect to all parameters of plant operation, Closer Supervision to enhance production efficiency and reduction of waste generation. Material Handling includes Material Tracking and Inventory Control to reduce overstocking of inventory and minimize waste by using the inventory on FIFO basis, Spill Prevention is done by conducting hazard assessment studies, using properly designed storage tanks and process vessels, equipping containers with overflow alarms being tested periodically, pipelines with valve lay out, installing interlock devices to stop flow to leaking sections and isolating equipment and process lines not in service. Material Handling and Storage Procedures in the raw material store includes adequate spacing between rows and drums, storage based on chemical compatibility, insulated electrical circuit, raising drum from the ground to prevent corrosion, material with identity tag with health hazard warnings, S.O.P with storage, handling and spill procedures and material safety data sheet available to all employees working with hazardous materials.(iv) Preventive maintenance once in a week can minimize waste generation due to equipment failure and subsequent generation of rejected products.[1]

5. WASTE MINIMIZATION METHODS BY RECOVERY AND RECYCLING:

The methods include direct use of waste material, recovering used materials for separate purpose, removing impurities from waste to obtain relatively pure substance.

5.1. Merits of recycling: (i) Reduces waste pollution leaving the plant. (ii) Control of reclaimed material purity. (iii) Reduces cost of transported waste to off-site. (iv) Lower unit cost of raw material.[1]

5.2. Demerits of recycling: (i) Increase of capital expenditure for recycling equipments. (ii) Additional operating and maintenance cost. (iii) Additional training of operator. (iv) More risk to workers.[1]

Process for solvent recovery from concentrated waste streams include Distillation,, Evaporation, Liquid- Liquid extraction, Sedimentation, Decantation, Centrifugation, Filtration and Adsorptive Bubble Separation Technology. Solvent Sublation is the non foam branch of Adsorptive Bubble Separation Technology which can be utilized for recovery of costly solvent Butyl Acetate from waste water of penicillin plant.[1,5]

5.3. **Importance of recovery and recycling in terms of economy of the industry** :(i) Control

environmental pollution, thus prevent the penalty imposed by pollution control board.(ii) Costly organic solvent recovered can be reused as starting and in process material.(iii)Increase the yield of production.(iv)Reduce the off-site transport cost.(v) Reduce the conversion cost of production in terms of labour, transport, electricity etc.

6. DIFFERENT TECHNIQUES AND EQUIPMENTS TO CONTROL POLLUTION OF PHARMACEUTICAL WASTE WATER:

6.1. Primary treatment for removal of suspended solids: The process involves removal of large suspended solids and trash from pharmaceutical effluent water by screening devices known as Bar Screens. The waste water is then allowed to follow sedimentation in large pre-designed sedimentation tanks by using thickeners and flocculating agents. Flocculation agglomerates very fine particles and enhances the rate of settling by gravitation. The most popular coagulating agent is Alum, $Al_2(SO_4)_3.18H_2O$. Aluminium ion reacts with the alkalinity of water to form alum floc. An alum dose of 10-50 mg per liter mixed with a polymer is used to enhance the settling rate at PH-5.50-7.00.The other coagulants are Iron salts like Ferrous Sulphate, Ferric Chloride; ferric ion is effective at PH 5-9. Activated Silica sol are found to be used as both coagulating as well as flocculating agents. Activated Silica sol of 20-30% of alum dose is used for coagulation. The coagulation and flocculation equipment consists of a tank equipped with impeller to provide the necessary contact between the coagulating chemicals and the waste stream .Coagulation reactions are as follows.[3]

$$Al_2(SO_4)_3 + 3Ca(HCO_3)_2 = 2Al(OH)_3 + 3CaSO_4 + 6CO_2$$

$$Al_2(SO_4)_3 + 3Na_2CO_3 = 2Al(OH)_3 + 3Na_2SO_4 + 3CO_2$$

$$Al_2(SO_4)_3 + 6NaOH = 2Al(OH)_3 + 3Na_2SO_4$$

$$Al_2(SO_4)_3.(NH_4)_2SO_4 + 3Ca(HCO3)_2 = 2Al(OH)_3 + (NH_4)_2SO_4 + 3CaSO_4 + 6CO_2$$

$$Al_2(SO_4)_3.K_2SO_4 + 3Ca(HCO3)_2 = 2Al(OH)_3 + K_2SO_4 + CaSO_4 + 6CO_2$$

$$2NaAlO_2 + Ca(HCO3)_2 + 2H_2O = 2Al(OH)_3 + CaCO_3 + CaCO_3 + Na_2CO_3$$

$$FeSO_4 + Ca(OH)_2 = Fe(OH)_2 + CaSO_4$$

$$4Fe(OH)_2 + O_2 + 2H_2O = 4Fe(OH)_3$$

$$Fe_2(SO_4)_3 + 3Ca(HCO_3)_2 = 2Fe(OH)_3 + 3CaSO_4 + 6CO_2$$

6.2. Dissolved-Air Floatation (DAF) Method For Primary treatment of pharmaceutical Waste Water: This method is the macro flotation branch of Adsorptive Bubble Separation Technology where hydrophobic oil and grease from maintenance and cleaning of pharmaceutical machines and equipments as waste having specific gravity equal to or less than that of waste water are selectively adsorbed or attached on the surface of the rising air bubbles and separated at the top of the column as a float. The floatation can be enhanced by addition of coagulant.[3,6,7]

6.2.1. Advantage of Dissolved Air Floatation: The space required for installation is very less. There will be five to six fold reduction in area if dissolved air floatation is used instead of gravity separation.

Floatation application on pharmaceutical waste water can be determined by simple sedimentation test by keeping the effluent water in a graduated cylinder and observing the movement of solids tend to float or remain in suspension, or if after addition of coagulant the resultant floc does not settle at a measurable rate. If this happens, then there is good possibility of application of Dissolved Air Floatation on the line of waste water stream. Dissolved Air Floatation are classified into Total Flow Pressurization, Partial Flow Pressurization and Recycle Flow Pressurization. Total Flow Pressurization is the simplest method found to be useful at the maximum limit of volumetric flow rate of 5,000 gallons per minute with a back pressure of air of 30-40 psig at the base of the column. Partial Flow Pressurization is employed for large and variable flow for which amount of pressurization is 25-50% of Total Flow [3]

Type. Recycle Flow Pressurization is applicable only in case of partial flow pressurization where recycling and pressurizing is done on a portion of effluent waste water from the floatation unit.

6.2.2. Design criteria of application of floatation unit:(i) Surface Over Flow Rate (ii) Surface Activity Of the Macro Particulate Waste in effluent water for being adsorbed on the bubble's surface .The surface activity can be increased by using a surface active agent in a concentration below C.M. C. (iii) 3% (v/v) of air is effective for floatation of grease and oil. A gas/solid ratio of 0.04 is the Thumb Rule of application.

With primary treatment, BOD load of pharmaceutical waste water can be reduced by 30-40% of the total BOD load.[3]

6.3. Secondary biological treatment for removal of organic matter:

Biological treatment of pharmaceutical waste in water are applicable for suspended and dissolved organic matter. They can be easily oxidized biologically, while others require special techniques. The food value of aerobic bacteria equivalent to the strength of waste is expressed in terms of 5 day biochemical oxygen demand (BOD_5).With secondary treatment, BOD load is further reduced to 30-35%.

The aerobic micro organism utilizes the pharmaceutical waste as their nutrient with the help of their metabolic pathways and enzymes secreted by the microbes cause digestion of waste material. The hazardous materials are oxidized to non hazardous forms by aerobic organisms.[3]

6.3.1. Activated Sludge method:

It is the biological treatment process where activated sludge of aerobic microbes is continuously mixed with the flow of pharmaceutical waste water in an aeration basin and continuous oxygen is supplied to the mixed liquor by diffused compressed air or by agitation

with impeller. The activated sludge is finally separated by sedimentation in a clarifier and part of the sludge is recirculated to maintain Mixed Liquor Suspended Solid (MLSS) for further activation of the process. The active biomass (sludge) metabolizes organic wastes consuming accelerates further removal of BOD from pharmaceutical waste water. The process has a number of advantages and disadvantages. [3]

dissolved oxygen and releases carbon dioxide producing new microbial cells. Protozoa utilizes some new bacterial cells as food for their growth. The recycling of sludge helps in initial build up of high concentration of microorganism in the mixed liquor to maintain MLSS which

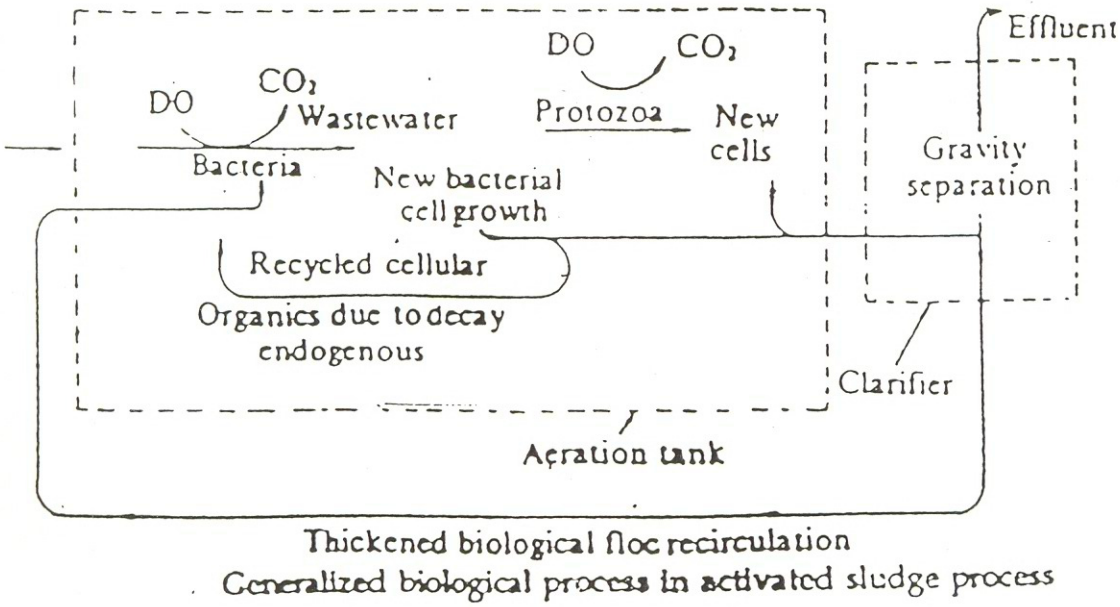

Fig 1. A schematic diagram explaining the Activated Sludge Removal of Bio-pollutants

6.3.2. Trickling Filtration method:

It is the modified Activated Sludge process where crushed rocks such as granite or lime stone are coated with light growth of bacteria and organic matter are adsorbed and oxidized by dissolved oxygen. The mechanism is similar to Activated Sludge method. The method is suitable for dissolved and colloidal organic matter. The BOD removal capacity is less than that of Activated Sludge method due to less time of contact with the bacterial flora. [3]

6.4. Tertiary treatment of pharmaceutical waste water:

This is the ultimate treatment of pharmaceutical waste water after secondary biological treatment followed by sedimentation, sludge digestion and sludge disposal. The tertiary treatment includes deionization by ion active resin, membrane filtration for deionization as well as removal of micro organism, the final effluent can be reused in pharmaceutical plant for production purpose. [3]

6.4.1. Deionization Plant of Ion Exchange Resin: Deionization of industrial waste water by ion exchange resins is based on the principle of strong electrostatic coulombic attraction between the ionic functional group of cross-linked hydrocarbon matrix of ion exchange resins and the opposite cations(C^+) and anions (A^-) present in waste water. Resins used now a days in pharmaceutical plants for demineralising water are cross-linked hydrophobic poly electrolytes of three dimensional net work of hydro carbon chain. They are polystyrene beads of sulphonic acid and ammonium compounds. The cation exchange resin contains anionic attracting groups like $R\text{-}SO^{3-}$, $R\text{-}COO^-$, $R\text{-}PO^{2-}$ etc for removal of cations in water, while the other counter part has attracting groups like $R\text{-}NH_3^+$, $_R{}^R\rangle NH_2^+$ etc for removal of anions in water. Ion exchange resin beads act as mobile ion exchangers. The ion exchange reactions in each column are as follows:

$R\text{-}H^+$ (generated cation exchanger) + C^+ (cation in water) ↔ $R\text{-}C^+$(exhausted) + H^+

R^+OH^-(generated anion exchanger) + A^-(anion in water) ↔R^+A^-(exhausted) + OH^-

$R\text{-}C^+$(exhausted)+ $H^+(H_2SO_4/HCl)$↔ $R\text{-}H^+$(regenerated for further removal).

R^+A^-(exhausted) + OH^- (NaOH) ↔ R^+OH^- (regenerated for further removal)

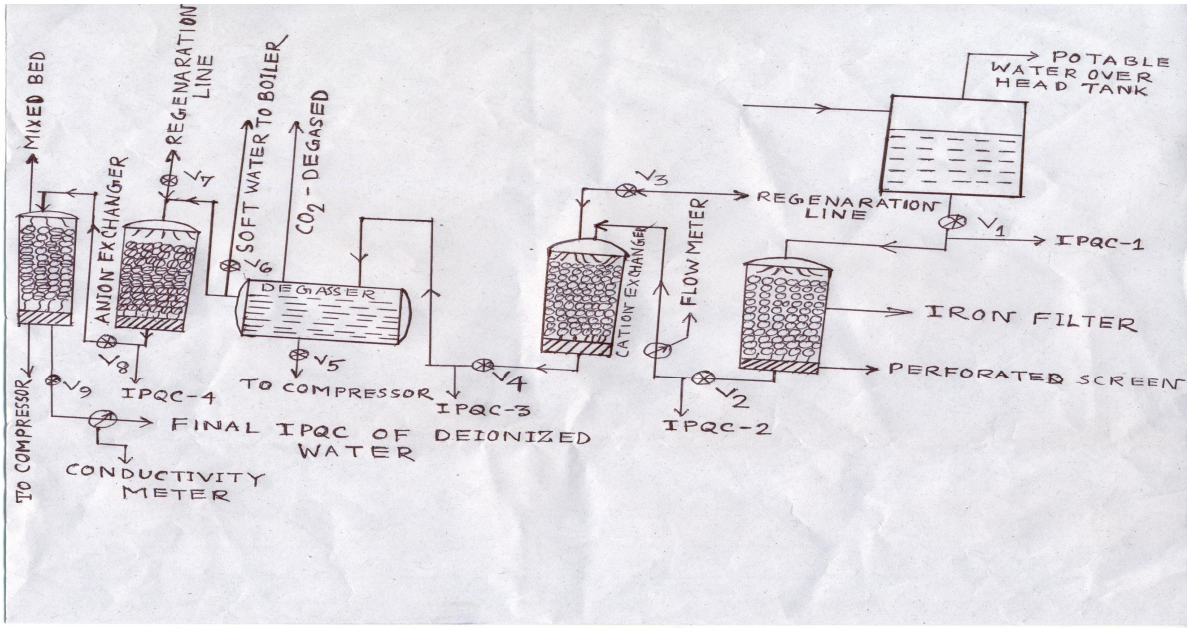

Fig 2: Schematic Diagram of Large Scale Deionization Plant in a Pharmaceutical Industry.

Deionization of waste water after secondary treatment of Demineralizing Plant or DM plant is the common process for removal of dissolved solids (salts-C^+A^-) and ions to obtain the desired pH[6.8-7.0] and electrical conductivity of waterexpressed in micro seimens[µs]. This water after passing through ultra violet radiation can be used for the production of liquid oral preparation. The process involves initial removal of iron from waste water by iron removal filter, removal of cation by sulphonic cation exchanger bed regenerated with either HCL or H_2SO_4, degassifier for removal of H_2CO_3(dissolved CO_2) just after cation exchange bed, then water enter into anion exchange bed regenerated by NaOH and finally mixed bed containing both cation and anion exchange resins for final clearance .This water is used as feed for multi column distillation plant as well as for production of non sterile pharmaceutical formulations. The water is pharmaceutically defined as purified water. [3]

6.4.2. Membrane deionization by Reverse Osmosis:

Reverse osmosis is the most popular membrane deionization as well as micro organism removal process where effluent water is forced through a semi permeable membrane under pressure (200-600 psi).This unit operation can replace distillation and deionization in a modern pharmaceutical plant and reduce the cost of production .T his is commercially viable for an intravenous fluid 6.4.3.plant. By changing the semi permeable membrane and application of pressure, quality of water can be varied. The driving force of this unit operation is proportional to the pressure differential minus the difference in osmotic pressure (ΔP-$\Delta\pi$). [8]

6.4.4. Adsorptive Bubble separation technology for treatment of pharmaceutical waste water:

The generic name was first proposed by **Lemlich in 1966** as **Adsorptive Bubble Separation Method** and included in **IUPAC** system of nomenclature in **1967.** The method is based on the differences in surface activity of the material being adsorbed on the bubble's surface and get separated on the top of the column. Materials which are molecular, colloidal or macro particulate in size known as **colligends** are selectively adsorbed chemically or physically on the air- water inter faces of rising bubbles through liquid column and is thereby concentrated and separated. Surface active agents which help to enhance the surface activity of the waste and thereby adsorptive separation at the gas-liquid interface are known as **collectors**. The cationic surfactant will adsorb anionic pollutant by counter ionic electro static attraction and vice versa. The different modes of operation of this technology are simple batch, simple continuous flow, continuous flow enriching by reflux, continuous flow stripping, combined enriching and stripping and staged

operation. The principle of this technology is based on Gibb's Equation of adsorption at gas-liquid interface. The technology is divided into two main branches of foam and non foam separations respectively. In foam separation branch, the different members are Foam Fractionation, Froth Flotation, and Micro Gas Dispersion. Froth floatation is sub divided into Ore Floatation, Micro Floatation, Macro Floatation, Precipitate Floatation, Ion Floatation, Molecular Floatation, and Adsorptive Colloid Floatation. Foam Fractionation separates dissolved waste materials in low concentration, while Froth Floatation separates insoluble waste materials from waste water. Solvent Sublation and Bubble Fractionation are the non foam separation branches of the technology. In foam separation, foam is the active carrier of the separated substance at the top of the liquid column. In bubble fractionation, the separated substance is carried by the rising bubbles by adsorption followed by deposition at the top of the liquid as the bubbles exit. Solvent sublation is the similar mass transfer of waste from pharmaceutical waste water to the interface of water immiscible liquid placed atop the waste water. As previously discussed, macro floatation can be successfully applied for removal of oil and grease from pharmaceutical waste water, foam fractionation is used for removal of heavy metals like Zn (ii), chromium (vi), cadmium (ii).Froth Floatation can be used for waste water purification by removing toxic in organics like mercury, lead and cadmium. Heavy metals are removed successfully by froth floatation using surface active agent like N-monodecanoyl diethylene triamine. Benzyl penicillin has been recovered from fermentation broth by using foam fractionation method. In most of the cases, non foam process is better suited for waste water treatment since procedures to collapse and dispose wet foams are not needed. By solvent sublation, varieties of toxic organics like 1,1,1-trichlorethane, dichlorobenzene, nitrophenol, naphthalene, phenanthrene and several phenolic compounds have been separated from waste water by different complex forming surface active agents using immiscible solvents like 1-octanol, 2-octanol, hexane, mineral oil and decyl alcohol.[6,7,9,11,12,13,14,15,16,17]

6.4.4.1. Performance criteria of waste removal by foam separation method:

Concentration of collector.(ii) Collector-colligend(waste) ratio(φ)(iii) Colligend concentration.(iv)Pulsed addition of collector.(v)PH.(vi)Ionic strength.(vii)Temperature.(viii)Gas flow rate.(ix)Presence of auxiliary agents to enhance adsorption at the gas-liquid interface.(x)Surface area of bubbles.(xi)Foam height and density.(xii) Foam drainage. (xiii) Equipment design. [6, 9]

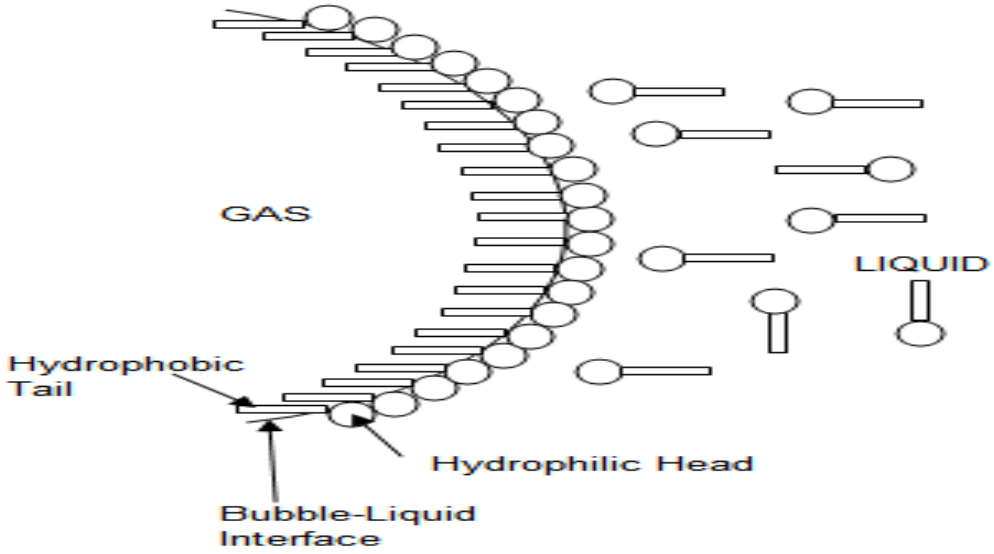

Fig 3: Cross Sectional View of a Bubble-Liquid interface of Surface Active Molecules being adsorbed by Adsorptive Bubble Separation Technology.Diagram adapted from Lemlich[1968]

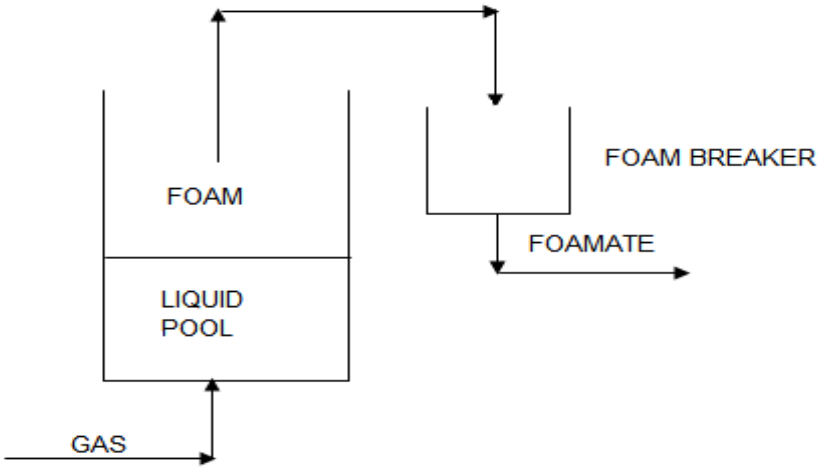

Fig 4: Schematic Diagram of a Batch Foam Fractionation Column in Operation. Diagram adapted from Lemlich [1972]

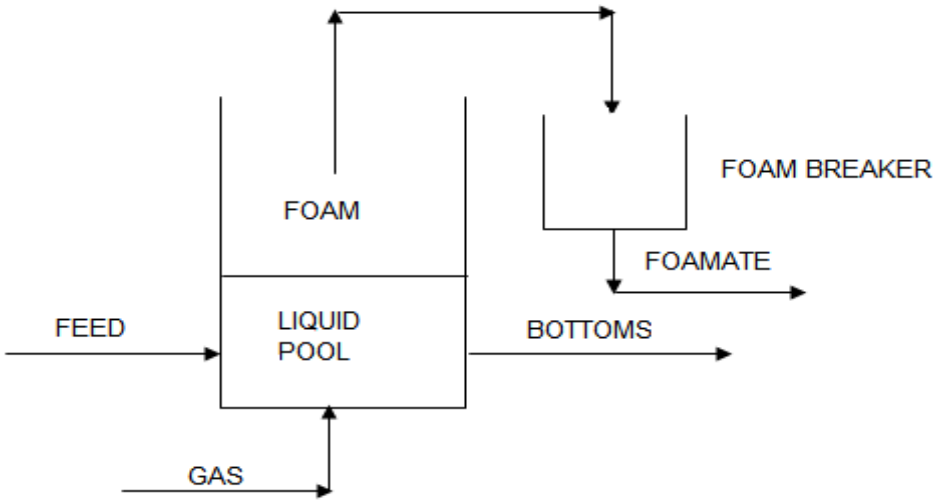

Fig 5: Schematic Diagram of a Continuous Foam Fractionation Column in operation. Diagram adapted from Lemlich [1972]

6.4.4.2. Collectors essential for removal of pollutants by Adsorptive Bubble separation technology:

Surface active agents:

Cetyl trimethyl ammonium bromide, Sodium lauryl sulphate, N-heptyl-L-hydroxy proline, Dodecylbenzene sodium sulphonate, Lauryl pyridinium chloride, Sodium laurate,Octadecyl trimetyl ammonium chloride, Dodecyl amine, Hexadecyl trimethyl ammonium bromide and Tetradecyl trimethyl ammonium bromide.[6,9]

6.4.4.3. Chiral collectors: Cyclodextrine, Alkylated amine acids, Digitonin, Vancomycin Rifamycin-B (1)

6.4.4.4. Molecularly imprinted polymers: Acrylic Polymers. [6, 9]

6.4.4.5. Advantages of non-foam Solvent Sublation method for purification of industrial waste water:

It is the advantageous non foam method for removal of organic waste from pharmaceutical /chemical waste water. The method combines the benefits of bubble fractionation and liquid - liquid extraction where no mixers, settlers and subsequent down stream treatment are not required.

Removal efficiency of volatile and non volatile organics from pharmaceutical waste water by solvent sublation has been found to be higher

than that by air stripping and conventional liquid - liquid extraction. The method can be used for higher degree of fractional recovery of recyclable waste. Sublation efficiency is found to be less dependent on column diameter. [11]

6.4.4.6. Factors influencing the separation of pollutants of waste water by solvent sublation:

(i)Addition Of water miscible alcohol in waste water produces smaller air bubbles which increases the water interfacial area to enhance the sublation efficiency.

(ii)Higher concentration of alcohols enhances the aqueous solubility of the hydrophobic compound, thereby reduces efficiency of the removal.

(iii)The presence of salts leads to decreased bubble's radius and thus reduces water interfacial area. It also reduces solubility of the hydrophobic compound leading to hastened removal of pollutant by sublation.

(iv)Small amount of surfactant like Sodium Dodecyl Sulphate (SDS) increases the removal efficiency by decreasing the bubble's radius.

(v) The effects of alcohols and salts are opposite in case of ion surfactant complex and that for neutral species.[6,9,10,11,12,13,14,15,16,17]

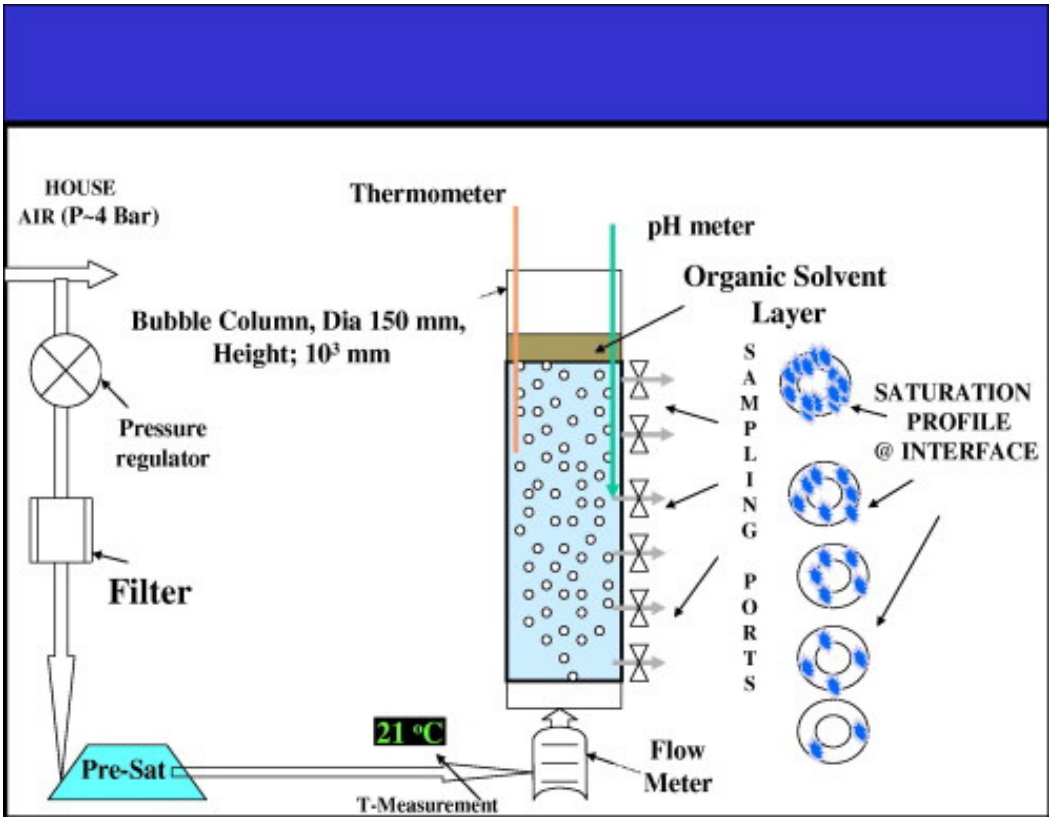

Fig 6: Schematic Diagram of a Batch Solvent Sublation Column in operation. Diagram adapted from [10]

6.4.4.7. Mass transfer mechanisms in solvent sublation:

Transport by air bubbles: Here, the transport of air bubbles is unidirectional in nature. Pollutants of volatile and non volatile in nature in waste water partition into and on the surface of the rising bubbles. Extent of partitioning can be explained by Henry's Law. The extent of partitioning of pollutant by sublation can be determined by equilibrium between bulk phase partitioning and surface adsorption with the help of mass balance equation of total mass of pollutant. The equation of mass balance is as follows.[11]

$$M = 4\pi r^2\tau + 4/3\pi r^3 C_A \quad \text{(I)}$$

Where, **M**= Total mass of pollutant in waste water, τ= concentration of pollutant at bubble's surface, C_A= concentration of pollutant in air bubble, **r**= bubble's radius.

At equilibrium, all the concentrations of pollutants stated above are related to the bulk phase water concentration of pollutant:

$$\tau = K_A C_W \quad \text{(ii)}$$

$$C_A = H_C C_W \quad \text{(iii)}$$

Where, K_A= Interfacial partition coefficient, H_C=Henry's law constant, C_W=concentration of pollutant in bulk water phase.

The effective concentration of pollutant (C_E) separated by each air bubble through sublation can be written as:-

$$C_E = M/4/3\pi r^3 = (3K_A/r + H_C)C_W = HC_W \quad \text{(iv)}$$

Where, **H**=Effective Henry's law constant. H/H_C is known as Enhancement Factor of sublation (ϵ_H).Effective Henry's constant relates inversely to the radius of the air bubble.

From known values of H_C and K_A for a particular pollutant, we can increase the enhancement factor of sublation by decreasing the bubble's radius.[11]

Bubble wake entrainment:- It is the second most important transport mechanism of solvent sublation. Wake is a small quantity of water of hemispherical shape which resides behind the rising bubble and enters into the water immiscible solvent along with the rising bubble.

The droplet of pollutant enters into the solvent, while droplet goes to the aqueous phase with an equilibrium amount of pollutant. The wake uniformly surrounds the bubble and the volume of the wake is $4\pi r^2 d_w$, where d_w is the wake's thickness.[11]

Solvent - water interfacial molecular mass transfer: Immiscible organic solvent-water interface is the main area of mass transfer. It is actually the molecular mass transfer mechanism conventional liquid-liquid extraction. [11]

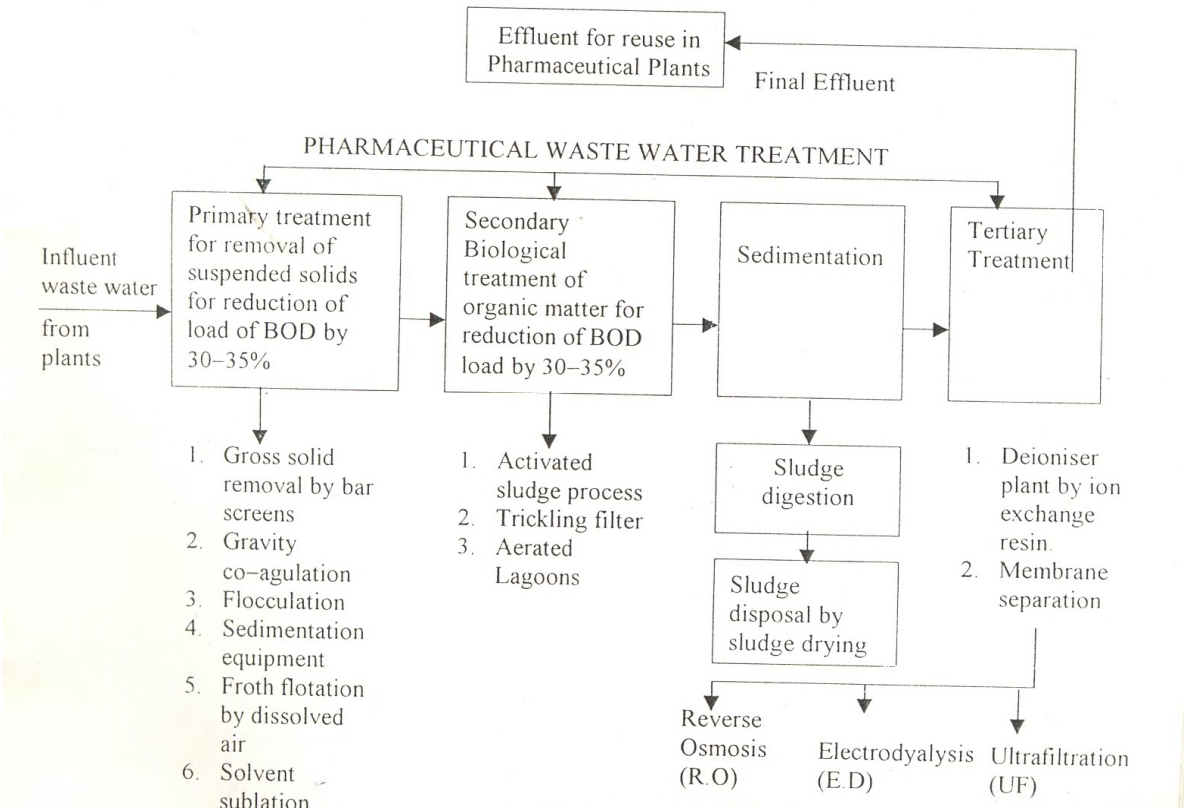

Fig 7: Process Flow Diagram for Purification of Waste Water in a Pharmaceutical Plant.

CONCLUSION:

This article may be a useful guide to the technical experts of professional pollution control agencies and technologists in pharmaceutical industries. The pharmaceutical industry in developing countries have shown a tremendous growth in last few decades. Manufacturing practices have been updated to the current G.M.P. to optimize the quality of medicines. Uncontrolled toxic pollutants and wastes those are discharged by these plants in air and water destabilize the human and aquatic system by creating a variety of health hazards and disturb the ecological balance of the world. So, treatment of effluent is a mandatory task. The governments of developing countries have not established the strict pollution control norms to the pharmaceutical industries as a result of which professional pollution control agencies have never targeted the pharmaceutical companies in true sense to solve the pollution problem. The pharmaceutical companies need to contact with pollution control expert who have upgraded their expertise rather than trying to have solutions on their own. The guidelines for pollution control should emphasize much on waste control from source and recycling rather than using costly

pollution control equipments for cost minimization. Profit making tendency and lack of technological knowledge are the causes of avoiding this deliberation. Pollution control is a specialized field, pollution control agencies will have to upgrade their expertise to tackle the problem and controlling authorities make laws more stringent. The problem will be better managed, if pharmaceutical companies keep a pollution management company as a partner.[2]

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