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Review Article

Technical Challenges in Pharmaceuticals and Cosmetics Industries in Nigeria: A Review of the Roles of Membrane Technology

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ABSTRACT

Pharmaceutical and cosmetic industries are being confronted with new and increasingly complex technical challenges, such as emulsion stability, metals impurity, air bubbles, hydration, and thickening. These technical challenges often result in the high cost of production, and waste of time, energy and raw materials. Over the years, a variety of research efforts has been made to address these challenges. Membrane technology is one of the promising approaches to solve these challenges. Membrane separation technology is a rapidly growing technology with much better flexibility, energy efficiency, and space economic than the traditional equipment currently used in these industries. This paper, therefore, looks into the possible applications of membrane technology in the pharmaceuticals and cosmetics industries. Specifically, issues of emulsions stability, the problem of thickening and hydration, and metals impurities are discussed. Then, the possible applications of the membrane in addressing these issues are presented.

Keywords: Pharmaceuticals; Cosmetics; Complex technical challenges; Membrane technology; Metal impurities

INTRODUCTION

Nigeria has a growing pharmaceutical market in West Africa with over 115 registered manufacturers [1]. The contribution of pharmaceutical industries in the provision of safe, pure, quality and efficacious products in healthcare delivery cannot be over-emphasized [2]. Pharmaceutical manufacturers' responsibility, therefore, is to ensure that all finished product is of high quality and fit to be used by the general public. This is because consumers cannot easily determine which products are fit by merely reading the labels.

Siti et al. [3] stated that the cosmetic industry is of the most stable industries despite the economic downturn because of the demand for its products which keep increasing every time. A cosmetic is defined as a substance or preparation used in contact with various parts of the human body such as epidermis, hair, nails, lips and external genital organs (external parts) or applied to the teeth or mucous membranes of the oral cavity with a view or for the purpose of cleaning, perfuming, protection, changing their outlook, converting body odors and keeping the surfaces in good condition [4]. Therefore, cosmetics products applied to human skin, mucous membrane (lips), hair and nails should be free from any hazardous substances and safe for health [5]. Generally, it is revealed that most of these challenges are as a result of the technology being used during the processing. In several processing industries, separation technology is widely used to separate and, in some cases, to purify a particular component from the rest of the mixture. The target component might be the desired product or an unwanted component, separated to increase the purity of the original mixture [6].

The Adoption rates of membrane technology in the pharmaceutical industry are growing at a fast pace as manufacturers recognize the benefits offered by membranes. Membrane technologies are increasingly becoming useful components of pharmaceutical production processes. For some time, membrane separation technologies of reverse osmosis, ultrafiltration, and microfiltration have been used to concentrate and purify both small and large molecules. More recent applications of membrane technologies have covered a broad range of industrial separation, concentration and purification needs [7]. Membrane separation technologies applications could be found in bio-pharmaceutical separation and purification operations via microfiltration, ultrafiltration and diafiltration [8]. Membrane filtration techniques

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of reverse osmosis and nanofiltration when combined with bioreactors and advanced oxidation processes could be used in pharmaceutical wastewater treatment [8]. The main interest of this review is to provide an overview of the potential applications of membrane technology in solving the challenges of metal impurities, emulsion stability, and thickening and hydration that are encountered in pharmaceutical and cosmetics manufacturing processes.

EMULSIONS STABILITY

In the pharmaceutical and cosmetic industry, one of the major challenges is the emulsion stability. Emulsions are found in every aspect of daily lives. The development and processing of emulsion have varieties of used both naturally occurring and as well in the manufacturing industries (Pharmaceuticals, Cosmetics, Agrochemicals, and Petrochemicals Industries) [9].

An emulsion can be defined as a biphasic system of a mixture of two immiscible liquids [10], one of which is uniformly dispersed in the other in the form of small droplets or particles. And since most emulsions are naturally or thermodynamically unstable, there is a need for chemical assistance (emulsifiers or surfactant to be added). Emulsifier stabilizes the system by forming a thin film around the globules of the dispersed phase [10].

An emulsifying agent when added tends to form a film around the globules (of size 0.25 μm to 25 μm diameters) of the dispersed phase. And either the dispersed phase or the continuous phase may vary in consistency from that of a mobile liquid to semisolid [11,12]. Therefore, pharmaceutical emulsions said to range from low viscosity (lotion) to high viscosity (cream). And the particle size of the dispersed phase commonly ranges from 0.1 μm to 100 μm [13].

The use of colloids mills and in line mixers is said to be a popular way to prepare and process emulsion. The two general types of pharmaceutical emulsion are oil-in-water (O/W) and water-in-oil (W/O) emulsion. In Oil-in-water emulsion, the internal phase or dispersed phase is said to be oil or miscible liquid and the external phase or continuous phase is reported to be water miscible liquid. And it is mostly formed when the aqueous phase constitutes more than 45% of the total weight of the mixture [12]. Furthermore, of the characteristics features of emulsion is-greasy effect, positive conductivity test as water, a good conductor of electricity at the external phase. And lastly, water-soluble drugs are more quickly released from O/W emulsion [10]. Moreover, O/W emulsion can be prepared by dividing the oily phase completely into minute globules surrounding each globule with an envelope of an emulsifying agent and later suspends the globules in the aqueous phase [14].

In a water-in-oil emulsion, the internal phase or dispersed phase is the water like liquid, while the external or continuous phase is the oil-like liquid [12]. W/O emulsion is useful in cleansing the skin of oil-soluble dirt. They are greasy, insoluble in water and oil soluble drugs are released from water-oil emulsion [10]. The W/O emulsion, unlike O/W emulsion, is prepared by dividing aqueous phase completely into minute globules surrounding each globule with an envelope of an emulsifying agent and finally suspending the globules in the oily phase [14]. Other types of emulsion are multiple emulsion (O/W/O), microemulsion, and Pickering emulsion [10]. Good quality of emulsion products depends on their stability. And generally to examine the emulsion stability is not easy [15].

- Some properties of a stable pharmaceutical emulsion are:
- Must be free from the coalescence of the dispersed phase
- An absence of creaming effect on the internal droplets
- Must be stable at the various temperature
- It should be not regarded by microbes on storage
- It should not have an unpleasant smell or degraded due to oxidation
- And lastly, it must be able to retain its physical characters like elegance, odor, color, and appearance [10,12]

Instability of emulsion consists of four different droplets mechanisms, namely creaming and sedimentation, flocculation, Oswald ripening and coalescence

CREAMING AND SEDIMENTATION

This is referred to as the most commonly encountered instability in the emulsion. Khan et al. [10] defined this encounter as the process where the oil phase separates out, forming a layer on the top of the emulsion. The process is said to results when the external forces such as gravitational or centrifugal forces cause two liquids of different densities to form in layers. This later makes the oil layer to build up the emulsion. It is; therefore, acknowledge that creaming could be minimized if the viscosity continuous phase is increased [10].

FLOCCULATION

It refers to a group of the droplets coming together to form larger units without any change in their size [16]. And from another definition by Khan et al. [10], flocculation was defined as the coming together of small emulsion particles to form an aggregate which is re-dispersable upon shaking. It results when there is a weak, net attraction between droplets and arises through various mechanisms and discussion of which is beyond the scope of this work.

OSWALD RIPENING

Of the properties of the immiscible liquids is mutual solubility which when in a polydisperse emulsion, the smaller droplets dissolve with time and left their molecules to be deposited. This after some time, the droplet size of the molecule becomes a larger value [16].

COALESCENCE

This type of challenges occurs when there is a fusion of two or more droplets into larger ones from thinning and disruption of the liquid film between the droplets. And the forces that exist in the liquid film make the separator difficulties [16].

THE PROBLEM OF THICKENING AND HYDRATION

Conventional mixing is applied in the processing of pharmaceutical creams and ointment. Though the use of conventional agitators is the most applied technology, there are numbers of challenges associated with the use of this technology. Hydration and thickening and suspending agents are of the most difficult of all mixing operation [17]. In building up of agglomeration (form from the addition of water to emulsifier or thickener) which is difficult to break down often occurs during the processing. In addition to the problem that could be encountered during the processing of cosmetics products, oil phase ingredients can form lumps which require shear to disperse [17]. And lastly,

long processing time and additional equipment may be required to obtain a homogeneous and stable finished product.

METALS IMPURITIES

The pollution with heavy metals often found in cosmetics products is said to be unavoidable due to their natural occurrence [18]. It was reported by Orisakwe et al. [19], that traces of metals (such as nickel) are found in 61% of the local body cosmetics creams and lotions in Nigeria. Oyedeji et al. [20] stated that all the cosmetics emulsion from Nigeria contained iron resulting from the type of water used in the emulsion processes. And despite the detection of traces of heavy metals hazard, very little attention has been given to metal contaminations in cosmetics products in Nigeria and Sub-Sahara African region [19]. The sources of toxic metals found in cosmetics are either added intentionally, released by metal components used in technological processes or from the raw materials for processing [19,21]. The chemical substances including, toxic metals (cadmium, lead, nickel, iron, etc.) in excess or low level present in cosmetics products are creating danger to human health; that when they are absorbed through the skin in to the blood, accumulates in the body and causes the body system to be malfunctioning Borowska et al. [5] and Izah et al. [22] classified heavy metals as essential and non-essential heavy metals. The essential heavy metals despite their benefits to a living cell can as well be toxic when the concentration exceeds the tolerable limit for the organisms. And non-essential heavy metals could be toxic to cells of the body even at low concentrations.

Elemental impurities (such as Ni, Co, and Cr) presents in some of the lipsticks are considered major causes of allergies and Cd, Cr and Pb are carcinogenic when present in the body in high concentrations. Eventually, these impurities could be absorbed by the users' skin and could cause diseases [23].

From the analysis above, Sani et al. [4], concluded that no statistical differences were observed between the higher and lower price cosmetics products in terms of the metal analyzed. And this, however, shows there is danger in excessive use of cosmetic products (either of lower or higher prices) contaminated with toxic heavy metals as they may lead to a slow release of the metals into the human body and accumulate in body tissues and hence cause certain health complications.

Iwegbue et al. [24] investigated the concentrations and exposure risks of Cd, Pb, Ni, Cr, Cu, Co, Zn, Fe and Mn in some facial cosmetics in the Nigerian market. Here, samples of a popular brand of cosmetic facial products were collected from cosmetics shops in Abraka, Warri, and Benin City in the southern part of Nigeria. The facial cosmetics (classified to lipsticks, lip glosses, and balms, eye shadows, eye pencils, eyeliners, mascaras, blushes and face powders) when passed through flame atomic absorption spectrometry (PerkinElmer, Analyst 200, Norwalk CT, USA). In another work, the levels of toxic metals (Arsenic, Cadmium, lead, mercury, and nickel) were asserted in different cosmetics products including creams, lipsticks, and glosses sold at local shops in Lagos Nigeria. The work which was carried out by Adepoju et al. [25] asserted the concentration of metal impurities in the samples of the cosmetic products using a spectrophotometer. From the result obtained, the level of the metals was seen ranges from 0.006 to 0.207ppm. Adepoju et al. [25], therefore predicted that despite the low-level concentration of these metals, the continuous use of the cosmetic products contaminated with such metals may, however, cause a slow release of the metals into the human body and cause harmful effects to the consumer over time (Tables 1-4).

At the other side, the identification and quantification of elemental impurities in pharmaceuticals have been a challenge for many years as far back as the 20th century [26]. The potential presence of trace amounts of heavy metals in drugs products is a real cause for concern with regulators. Traces of metals such as cadmium, lead, and mercury, are likely to enter the manufacturing trends from natural sources [27]. Metals from manufacturing and processing equipment or rather catalysts being used have the potential to cause problems to the manufacturers. And most of the effort to secure these metals impurities through the use of Method II and inductively coupled plasma-mass spectrometry (CICPMS)

Table 1: Concentration (mg kg^{-1}) of some heavy metals in lipsticks and skin lightening creams in Kano [4].

Metals detected	Lipstick		Skin lightening creams	
	Higher price	Lower price	Higher price	Lower price
	Range (mg kg^{-1})	Range (mg kg^{-1})	Range (mg kg^{-1})	Range (mg kg^{-1})
Mn	4.91	19.61	12.25	4.71
Ni	7.35	11.03	7.35	7.35
Cu	8.47	8.47	0	4.24
Cd	0.56	1.39	0.76	1.11
Cr	0	0.05	0.05	0
Pb	0.1	0.19	0.09	0.09

Table 2: Concentrations ranges of metals (μg g^{-1} wet weight) in facial cosmetic products in Nigeria [24].

Product type	Cd	Pb	Cr	Ni	Cu	Co	Fe	Mn	Zn
Lipstick	3.0-37.3	11.6-18.0	17.1-115.8	17.0-37.9	1.1-135.4	4.5-19.9	421.6-44070	2.1-151.0	9.2-33.0
Lip gloss/lip balm	0.7-4.7	1.9-18.3	1.8-15.2	1.7-25.5	0.3-4.1	1.3-15.0	26.9-23072	0.28-106.7	5.4-40.4
Face powder	2.1-5.0	5.9-3399.9	4.6-232.5	5.3-27.7	1.4-23.4	5.2-15.2	157.3-47098	18.0-154.5	8.0-3300
Eye shadow	3.7-5.1	0.3-21.6	7.3-146.4	20.9-30.8	2.0-194.3	9.2-17.1	142.8-52036	2.4-159.1	8.6-414.8
Eye liner	2.8-13.5	9.6-322.5	4.0-19.1	18.4-68.8	1.3-10.8	5.2-103	421.6-44070	2.60-2102.58	9.2-33.0
Eye pencil	0.7-5.2	3.3-33.8	10.5-45.1	2.2-55.7	1.5-67.2	1.4-43.6	71.6-86466	107-456.2	107-456.2
Blush	1.3-4.8	12.1-378.0	9.9-41.1	3.3-25.3	0.7-5.2	2.5-12.0	115.4-77517	4.2-385.8	12.1-89.8
Mascara	1.8-5.1	5.4-18.5	5.0-21.3	10.3-588.5	1.6-16.9	4.6-16.6	142.8-68782	2.4-461.5	8.2-276.2

has low or no yields [26]. The testing protocol of United States Pharmacopeia (USP) being used as well is outdated as it is difficult to spot very low levels of the metals, it gives no indication of the number of metals that is present, or its identity [27]. Metals that could be found in pharmaceutical products (such as antimony, arsenic, bismuth, cadmium, lead, mercury, molybdenum, silver, tin and many more) and their possible concentrations could be found in Li et al. [27] works.

Awofisayo et al. [28], determined the composition of elemental impurities in pediatric powder for suspension (PPS) and double strength tablet (DST) commercial anti-malarial formulations of artemether-lumefantrine (AL). There were no significant differences in the levels of cadmium, lead, zinc and arsenic in the two types of formulations as observed in the sampled products but significant differences in the levels of chromium, nickel, and cobalt. The presence of metals such as arsenic, cobalt, and lead in the antimalarial product (such as Artemether-Lumefantrine) that are taken frequently especially in the malaria-endemic environment may pose some long term health risks. In similar research work, Orisakwe et al. [29], determined the concentrations of elemental impurities in 28 different brands of commonly used pediatric syrups, purchased randomly from patent medicine retail outlets in Port Harcourt, Rivers State, Nigeria. Some of the selected drugs as shown in Table 5 revealed the level of metals impurities in the selected drugs.

Furthermore, since the use of traditional and alternative medicine has increased worldwide, there would also need to mention the elemental impurities in some of these herbal products. Heavy metal traces can also be found in traditional medicine, of which its accumulation can be toxic to the body. Amadi et al. [30], determined the concentrations of mercury, antimony, and tin in orally administered herbal supplements commonly sold in Nigeria. The levels of the metals were later analyzed to ascertain their comparability with the recommended limits of the World Health Organization (WHO), European Union (EU) and the United States Environmental Protection Agency (USEPA). Table 6 shows the mercury, antimony and tin levels (mg/l) of Nigeria herbal supplements (NHS) respectively in comparison with recommended guidelines of WHO. And it could be deduced from the table, that only the Antimony did not violate the permissible limit of WHO limit of 0.005 mg/L which to say Nigerian herbal supplements had high concentrations of mercury and tin, most especially the solid dosage forms (caplets, capsules and soft gels) which may be toxic to living tissue when accumulated in the body. The International Council of Harmonization (ICH) categorized the various element impurities in pharmaceutical industries in four different classifications which were considered to facilitate decisions during the risk assessment.

Ullah et al. [31] stated that heavy metals which includes: antimony, arsenic, bismuth, cadmium, cerium, chromium, cobalt, copper, gallium, gold, iron, lead, manganese, mercury, nickel, platinum, silver, tellurium, thallium, tin, uranium, vanadium, and zinc are those whose density is five times greater than the density of water. And when these essential metals present in higher concentration become toxic and serious threats to the society and consumer and a more-quantitative method would be a huge improvement [31]. Mercury content in pediatric syrups may constitute a significant source of heavy metal exposure to children and may be of public health importance in Nigeria [29]. Therefore, since it will be most difficult for consumers to trace out products containing metals and other harmful chemical substances by reading the labels. It is, therefore, the responsibility of the producers to ensure that the products are free from metals impurities (Table 7).

Table 3: Concentration analysis of metals in cosmetic samples from local shops in Lagos [25].

Parameter	As	Cd	Pb	Hg	Ni
Number of samples with detectable metal	50	50	50	50	50
Minimum concentration of metal ion detected metal (ppm)	0.006	0.023	0.017	0.009	0.032
Maximum concentration of metal ion detected metal (ppm)	0.031	0.203	0.09	0.207	0.105

Table 4: Concentration of elements in Artemether-Lumefantrine [28].

Metal	The concentration of element × 10^{-3} ppm, mean ±SD		
	DST*	PPS*	P-value
Cd	7.0 ± 3.4	4.8 ± 1.8	0.18
Pb	5.2 ± 2.2	4.0 ± 1.7	0.33
Zn	15.0 ± 3.2	8.7 ± 3.0	0.11
Cr	14.8 ± 3.6	8.7 ± 40	0.012
Ni	5.0 ± 2.6	2.2 ± 0.8	0.077
Co	3.0 ± 1.4	1.5 ± 1.1	0.028
As	1.2 ± 0.8	0.7 ± 0.5	0.22

*DST: Double Strength Tablet; *PPS: Pediatric Powder for Suspension

MEMBRANE SEPARATION

Membranes used to satisfy many of the separation requirements in the process industries can be defined as a thin layer of material

Table 5: Metal levels of selected syrup in Port Harcourt, Rivers State [29].

Drug name	Metal level (µg/g)		
	Antimony	Tin	Mercury
Amodiaquine (50 mg/5 mL) syrup	0.88	1.33	1.84
Paracetamol (120 mg/5 mL) syrup	0.95	1.11	2.57
Multivitamin syrup	0.71	0.89	1.58
Ampicilin/Cloxacillin (250 mg/5 Ml) oral syrup	1.04	1.86	4.87
Artemeter (15 mg/5 mL), Lumefantrine (90 mg/5 mL) oral suspension	1.14	2.05	4.94

Table 6: The concentration of Mercury, Antimony and Tin in Nigerian herbal samples [30].

S/N	NHS	Mercury			Antimony			Tin		
		Concentration (mg/L)	WHO (mg/L)	WHO (%violation)	Conc. (mg/L)	WHO (mg/L)	WHO (%violation)	Concentration (mg/L)	WHO (mg/L)	WHO %violation
1	Eroxil 5000	0.00488	0.001	388	0.0005	0.005	NIL	0.00327	0.002	63.5
2	Super bitter	0.00728	0.001	628	0.0006	0.005	NIL	0.00355	0.002	75
3	Super cleanser capsules	0.01945	0.001	1845	0.0024	0.005	NIL	0.00844	0.002	322

that will only allow certain compounds to pass through it [32]. Membrane materials can be made of polymeric materials, such as polyamide, cellulose acetate, polyethersulphone, or from ceramic materials such as aluminum oxide, zirconium oxide or silicon oxide [32]. The substances that will pass through are determined by the size and the chemical characteristics of the membrane and the material being filtered. In addition, the membrane can be homogeneous or heterogeneous, symmetric or asymmetric, solid or liquid; it can also carry positive or negative charges or can be neutral [33].

Membrane separation systems require no or very little chemicals compared to standard unit operations and are used for various separation of mixtures of gases and vapors, miscible liquids (organic mixtures and aquenyl organic mixtures) and solid/liquid and liquid (liquid dispersions and dissolved solids from the liquid) [34]. And are also easy to scale up, energy efficient, which are widely used in various industries such as wastewater treatment, beverages, and dairy, oil and gas, pharmaceutical and cosmetic industries, etc. [33]. Membrane technology also allows rooms for further improvement and integration in the development of better performing treatment technology unlike conventional techniques which has limited room for improvement as most of the technique are rigid and exacting [35]. Other advantages of the membrane over conventional techniques in industrial applications are presented in Table 8.

Table 8 shows the possibility of energy savings relative to competitive, thermally driven options by introducing membrane processes for separations and the need for a large-scale integrated systematic approach for the application of membranes in feed streams [36]. Membrane separation techniques are used in downstream processes for bio-pharmaceutical separation and purification operations via microfiltration, ultrafiltration, and diafiltration [37]. In the pharmaceutical and cosmetic industries, a range of filtration and membrane separation are employed to maintain product purity and product quality. Microfiltration is one of the applicable membrane systems in pharmaceutical, food and semiconductor industries and in wastewater treatment. They are applied in pharmaceuticals and cosmetic industry for sterile filtration, removal of heavy metals or hydroxides, and removal of oil-water effluents [34].

THE POTENTIAL OF MEMBRANE APPLICATION

Emulsion stability

Membrane emulsification technology is a drop-by-drop emulsification method through a porous membrane and has received increasing interest over the years as an alternative method to produce emulsions and particles especially in cosmetic and pharmaceutical Industries. Of the greatest result using membrane emulsion technology is the production of emulsions and particles with target size in the range of 10 μm to 100 μm, and size distribution with a coefficient variation Piacentini et al. [38]. Of the benefits of membrane emulsification mentioned in Piacentini et al. [38], includes; production of uniform particles, droplets size controlled by appropriate membrane pore size selection, low shear stress, energy requirement reduction, etc. The hydrophilic membrane is used to prepare oil-in-water, water-in-oil, water-in-oil-in-water, etc. emulsions. In such membrane, droplets are formed at the pore mouth of the membrane by forcing the dispersed phase to permeate through the membrane and stripping the droplets from the pore into the continuous phase by the action of the axial velocity without wetting the membrane (Table 9) [39].

A stability test was experimented by Laouini et al. [40] on two separate drugs (drug-free nanoemulsion and drug-loaded nano-emulsion) as shown in Table 6. At the end of 120 days, stability data for drugs shows that the Z-average size and the span factor remained nearly unchanged during the storage period. This demonstrates the good stability of the nano-emulsions and thus indicates an adequate formulation of the preparation and optimum process conditions.

Piacentini et al. [38], explained different patents on membrane emulsification process including membrane operation methods,

Table 7: Categorization of the various elemental impurities in pharmaceutical products according to ICH.

Class	Toxicity level and source	Metals Impurities
1	They have limited or no use in the manufacture of pharmaceutical but can be present as impurities (e.g. mine excipients) and cannot be readily removed from the material.	As, Cd, Hg, Pb
2	They come along with materials used to produce drug products.	V, Mo, Se, Co, Au, Ti, Pb, Ir, Os
3	They only found if intentionally added. And they have low toxicity and have high permitted daily (PDE) limits	Sb, Ba, Li, Cr, Cu, Sn, Ni
4	Low inherent toxicity, though their PDE are yet to be established.	Al, B, Fe, Zn, Na, Mn, Mg, W

Table 8: Advantages of membrane over conventional techniques.

Processes	Energy consumption		Membrane type	Conventional	Reference
	Membrane	Conventional			
Energy cost of providing pure water from ocean salt water	1 $KWhrm^{-3}$	640 $KWhr^{-3}$	Ideal de-mixing Membrane	Heat of Vaporization	[48]
Suspended particles and macromolecular solutes processing	7.6 Kwh/m^3	73 kwh/m^3	Micro/Ultra Filtration	Flash Evaporation	[49]
50 million gallons/day seawater processing	6.7 Kwh/m^3	78.5 Kwh/m^3	State-of-the-art Seawater Reverse Osmosis	Optimized Thermal Distillation Plant	[36]
Propylene/propane separation	0.050 kw h/lb	0.302 kwh/lb	Vapor Permeation Membrane	Cryogenic Distillation	[36]
CO_2 removal from oxygen-blown gasification	$ 41-47/ton	$ 48.3/ton	Microfiltration membranes	The amine absorption capture technology	[50,51]

membrane emulsification devices and different membranes that can be applied to understand the innovation potential of membrane emulsification technology and predict future research trends and activity in the emulsion process. Some examples of droplets that have been manufactured, the membrane emulsification method, membrane type, particle size and the field of application of the product are listed in Table 10.

Similarly, the size of the droplets is largely dependent on the size of the membrane pores, which means it is easy to select the membrane most suitable for the application [41]. A summary of typical results and conditions for producing some of the emulsions with narrow droplet-size distributions selected from the literature is presented in Table 11. Moreover, membrane emulsification seems will be a simple, effective and reliable technique for drugs and cosmetic processes.

Metal impurities removal

The use of water in industrial manufacturing processes varies considerably between sectors and processes. As a consequence of water usage in industrial processes, it may become contaminated and almost all the water taken into industrial processes ends up as wastewater [32]. Removal of heavy metals dissolved at low and high concentrations in water and wastewaters is often a problem that can be solved in different ways. Since one of the major sources of these metal impurities in manufacturing cosmetic and pharmaceutical products is from the water used. A membrane as a cheap retrofit system can be installed within the process for treating the water before being used for cosmetics and pharmaceutical production. In some methods for treatment of heavy metal ions, membrane separation is considered as a great promise technique, because of their high efficiency, easy operation, and space saving. In recent years, ultrafiltration (UF) or microfiltration (MF) membranes are used for Solid-liquid separation instead of clarifiers, because UF/MF membrane processes are much more compact and result in water with much better quality than clarifies. Therefore, Industrial wastewaters when treated with polymeric chelates and subsequently filtered through UF or MF membranes result in high metal removal and also higher membrane fluxes than those treated with commodity dimethyl dithiocarbamate (DTC) chemistries [42].

The submerged membranes utilized to process industrial wastewater containing heavy metals may have various types of physical and chemical parameters. With respect to physical parameters, in one embodiment, the ultrafiltration membrane has a pore size in the range of 0.003 to 0.1 um. In another embodiment, the microfiltration membrane has a pore size in the range of 0.1 to 10 Lum. Zhang et al. [43] demonstrated the great potential of Graphene Oxide framework membrane in heavy metals removal. The developed membrane was found to have a high pure water permeability of 5.01 $Lm^{-2}h^{-1}bar^{-1}$ and not only that, but it also has rejections towards Magnesium, lead, Nickel, Cadmium, and zinc (Tables 11 and 12) [43,44].

Ultrafiltration membrane, when enhanced with a polymeric material, tends to have high metals removal ability. Uludag et al. [44] investigated the Separation of mercury from aqueous solutions by continuous Polymer-Enhanced Ultrafiltration (PEUF). Polyethyleneimine (PEI) was added to the solutions as the complexion agent before circulating the solution in a laboratory scale continuous ultrafiltration system. The outcomes of the experiment as presented in Table 12 show that ultrafiltration, when enhanced with a polymer, yielded a better percentage of mercury retention.

Table 9: Stability data of the prepared nano-emulsions for storage temperature of 5°C and 25°C [40].

Time	Day 0	Day 45		Day 90		Day 120	
(a) Drug free nano-emulsion Storage temperature (°C)		5	25	5	25	5	25
Average size* (nm)	85 ± 2.5	8.5 ± 0.9	84 ± 2.1	85 ± 1.2	92 ± 0.6	89 ± 0.7	99 ± 0.8
Span factor	0.30 ± 0.01	0.31 ± 0.00	0.38 ± 0.01	0.25 ± 0.00	0.22 ± 0.01	0.22 ± 0.01	0.20 ± 0.01
Zeta potential* (mV)	-22 ± 0.8	-21 ± 0.5	-22 ± 0.6	-21 ± 0.7	-23 ± 1.4	-20 ± 0.5	25 ± 0.7
Time	Day 0	Day 30		Day 60			
(b) Drug-loaded nano-emulsion Storage temperature (°C)		5	25	5	25		
Average size (nm)*	106 ± 3.6	108 ± 1.6	109 ± 1.1	105 ± 0.5	102 ± 1.4		
Span factor*	0.31 ± 0.01	0.29 ± 0.01	0.27 ± 0.00	0.23 ± 0.01	0.22 ± 0.01		
Zeta potential (mV)*	-18 ± 0.5	-20 ± 1.0	-15 ± 0.3	-16 ± 0.2	-16 ± 0.3		

*Each value represents the mean of the 3 batches of reproducibility ± S.D. (n=3)

Table 10: Particles produced by membrane emulsification [38].

Final product	Dispersed phase	Emulsion	ME method	Particle size(μm)	Uses	Membrane
Solid lipid particles	Lipid phase	O/W	D-CF	0.1-0.5	Encapsulation	Ceramic
Simple emulsion	Squalene	O/W	P	0.135-0.220	Drug release	Polyrthersulfonate
Gas droplet	Gas	W	D	≥10	Ultrasonic contrast agent	SPG or Ceramic
Inorganic particles	Inorganic compounds	W/O	D-CF	0.1-50	Encapsulation	
Inorganic particles	silica	W/O	D-CF	0.01-500	Packaging encapsulation	Polyimide, Glass

D: Direct ME; P: Premix ME; CF: Cross-Flow ME; ME: Membrane Emulsification

The data indicated the various method open for the production of a variety of structure particulate materialsin the emulsified droplets, such as polymerization, gelation, evaporation, freeze-drying, solidification, crystallization, etc. that can be used individually or in combination to produce oil-in-water and water-in-oil emulsions (O/W,W/O), multiple emulsions(O/W/O,W/O/,solid–liquid microspheres, solid microcarriers, liposomes, etc

In other work, the rejection of chromate ions from portable water through indigenously developed polyacrylonitrile (PAN) based ultrafiltration membrane at low operating pressure was investigated. More than 90% of chromate ions were found rejected at pH ≥ 7 at a low chromium concentration (i.e. ≤ 25 ppm) in the feed. And this approached to beyond detectable limits for the concentration of 50 ppb. From the results obtained they evaluated the rejection coefficient in terms of flux, charge density, and membrane porosity. Finally, high recovery of chromate ions is said to be possible from processing water with the use of polyacrylonitrile ultrafiltration membrane (Table 13) [13].

Water-soluble polymeric ligands have shown to be powerful substances to remove trace metals from aqueous solutions and industrial wastewater through membrane processes such as ultrafiltration [45]. This was justified by Trivunac et al. [45] when the applicability and the efficiency of selected macro ligands (polyethylene glycol 5000 (PEG5000), diethylaminoethyl cellulose (DEAE23) and dextrin) in the removal of zinc and cadmium ions from the water have experimented. Their experimented work has presented in Table 6, shows that the diethylaminoethyl cellulose used in the research proved to be very effective, which may be supported by the high retention coefficients of both metal ions obtained, and could be a better complexion agent with ultrafiltration. The advantages of complexation–filtration process are the high separation selectivity due to the use of a selective-binding and low-energy requirements involved in these processes.

Supported Liquid Membranes (SLM) is another potential membrane that has proved to be effective not only for removing but also for the recovery of heavy metals from water [46]. The separation and transport of lead (II) ions made to pass through the liquid membrane based on triethanolamine (TEA) in cyclohexanone supported in microporous polypropylene films were seen to have 99.94% metal ions extracted across the membrane when 0.5M acid concentration was used in the feed phase with 3.75 mol/dm^3 TEA concentration in the membrane phase. And similarly, when higher concentration often was added, maximum metal ion was seen extracted. And with same or extractant membrane, other metal ions could be removed [46].

The removal of some heavy metals Cu(II), Cd(II), Mn(II), Pb(II) As(III), and As(V) from water solution using polymeric membrane techniques were discussed by Khulbe et al. [47]. For the Polymeric membrane, the end result showed removal efficiencies of some

Table 11: Typical results and conditions for producing emulsions with narrow droplet-size distributions [41].

Membrane	Norminal Pore Size (μm)	Surface Type	Experimented Condition	W/O or O/W	Droplet Size, d_p
Microporous glass	1	hydrophobic	Oil phase: soybean oil Water phase: water+egg yolk proteins	W/O	$3d_p$
Ceramic	0.1	hydrophilic	Oil phase: vegetable oil+8% v/v monoglyceride Water phase: skim milk Cross flow velocity 9 ms^{-1} Flux: 140 lm^{-2} h^{-1}	O/W	$3d_p$
Ceramic	0.2 and 0:5	hydrophilic	Oil phase: mineral oil Water phase: water+36.4% wt sorbital (70%)+2.16% wt dobanol 91-8+0.04% Wt formalin Flux: 7.4 lm^{-2} h^{-1} Cross flow velocity: 1 ms^{-1}	O/W	$4d_p$
SPG micro-porous glass	0.98, 2.70, 4.70	hydrophilic	Oil phase: toluene+2%-10% wt PE-64 copolymer	W/O	$<d_p$
Single glass capillaries	5-200	hydrophilic	Oil phase: mineral oil+3% wt iso stearic acid Water phase: water+3% wt triethanolamine +0.3% wt sodium nipastat Cross flow Velocity: 0.5 ms^{-1}	O/W	$4d_p$

d_p: membrane pore diameter

Table 12: Mercury retention using a complexed ultrafiltration system [44].

Feed Mercury Concentration (ppm)	PEI Percentage (w/v)	Permeate Concentration (ppm)	Retention
98.5	0.025	0.5	0.99
925.2	0.25	6.89	0.99

pH is 5, UF pressure is 100 kPa, and the feed flow rate is 0.048 m^3/h

Table 13: Effect of ultrafiltration membrane on the retention of metals using different complexing agents (p=300 kPa, pH=9.0) [45].

		Complexing Agents and their Metal Retention %		
Metal	Concentration of metal in the stream (mg dm^{-3})	Dextrin	PEG5000	DEA23
Zn (II)	50	10	90	99
Cd (II)	50	5	30	95

Table 14: Metals removal efficiency using absorption and nanofiltration membrane [47].

Metal Ion	Concentration (ppm)	Removal efficiency (%)
Cd	500	97
Cu	12000	99.9
Pb	0.64	84
As(III)	600	89
Mn	310	98

Table 15: Metals rejection in both of individuals and simultaneous at 25 mgL^{-1} metal ion concentration [14].

Metal ion	Nickel (II)	Copper (II)	Chromium (III)
Metal rejection (independently) wt %	95.1	98.6	99.1
Metal rejection (simultaneously) wt %	94.4	98	98.3

The process which was first carried out on separate metals and later in combined state, characterized by low energy of about 1 bar is found to have a rejection of 97.6%, 99.1% and 99.5% for Cu(II), Ni(II) and Cr(III) ions respectively at pH of 7. And this makes the membrane one of high selectivity for metal impurities separation

of the metals. It could be seen that Cu has the highest removal efficiency follow by the Mn. This absorbent membrane is a very significant economic, convenient and easy operation technique. And this could be seen from the result of the high metal removal efficiency and is applied as a quick method for all types of wastewater treatments (Table 14).

Similarly, Barakat et al. [14] investigated the applicability of the complexation polyethersulfone (FUS 0181) ultrafiltration membrane process for removal of toxic heavy metals [such as Cu(II), Ni(II) and Cr(III)] from water with the assist of Carboxyl methyl Cellulose to increase the molecular weight and size during filtration.

Another way which could be considered for rejecting or minimizing the contamination of metals impurities into the pharmaceutical and cosmetics processes is the use of the hybrid membrane in processing equipment. Hybrid membrane process also called integrated membrane processes, the membrane combined with other processes so that the hybrid process gives better performance compared to these processes used alone [32]. Hybrid membrane processes can be used for increasing the quantity of treated water, to achieve higher removal efficiency and cleaner products, and to reduce the need for membrane cleaning [48-51].

Juholin et al. [32] in his work, highlighted two major types of hybrid membrane processes: chemically or biologically enhanced membrane processes, reactive membrane. The chemically hybrid Membrane process is where chemicals or biological reactions are applied to achieve desired functionalities (e.g. Membrane bioreactor) while Membrane reactive hybrid are material shaving e.g. (photo) catalytic, adsorptive, magnetic or other functionality which enhances separation efficiency or productivity of the process (e.g. PS/TiO_2 composite nanofibre membrane) (Tables 15 and 16) [32].

Table 16: The rejection coefficients in the membrane distillation experiments [32].

Rejection Coefficients	As (µg/dm^3)	Cr^{6+} (µg/dm^3)	Ni^{2+} (µg/dm^3)
Feed	3600	3020	1668
Retentate	5670	4440	1915
Permeate	110.11	<0.80	<0.82
Rejection %	98.1	>99.9	>99.9

CONCLUSION

Compared with the original system, membrane technology based purification processes such as ultrafiltration and nanofiltration could save a lot of time, and reduces the level of metal impurities in water, especially when they are enhanced with other materials. In the past, workers had to clean plasma purification units and other purification equipment frequently. This takes a lot of time. Pharmaceuticals and Cosmetics processing types of equipment if enhanced with the membrane will reduce (to nontoxic level) the hazardous effect of impurities associated with pharmaceutical and cosmetic products and saved human resources to improve the economic efficiency of the factory. The future trends will be on how membrane technology can solve the problem of emulsion stability, thickening and hydration in Cosmetic and Pharmaceutical Industries, because they have not yet been fully demonstrated.

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