Recent progress in the hydrophilic modification of alumina membranes for protein separation and purification

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A membrane is defined as a selective barrier that allows certain molecules or ions to pass through by combining sieving and diffusion mechanism. Membranes also can be classified based on its materials, i.e. polymeric (organic) and ceramic (inorganic) [1]. It can be further categorised based on its permeability and structure, in which membrane permeability is defined as permeable, semi-permeable and impermeable [2] while membrane structure is defined to be either porous or dense. Currently, polymeric membranes are the leading membrane type in industrial applications. Meanwhile, ceramic membranes are mainly used in special cases where the application of polymeric membranes is deemed unsuitable and inapplicable. Polymeric membrane suffers from several problems such as proclivity to bio-fouling, low fluxes, low mechanical strength and restricted chemical and thermal stability [3]. As a result, ceramic membranes have been seen as the best candidate to replace polymeric membranes in harsh condition applications due to their capability of working in acidic or basic conditions [4].

Ceramic membrane is made from inorganic materials, generally metal oxides and non-oxides. Widely used metal oxide materials are alumina (Al₂O₃) [5], titania (TiO₂) [6], silica (SiO₂) [7] and zirconia (ZrO₂) [8], while non-oxide materials [9] refer to silicon carbide and silicon nitride. Generally, ceramic membranes have great mechanical strength as well as high thermal and chemical stability [10,11]. For most of the applications, alumina is used due to economical material [12] and enable the use of high trans-membrane pressures and reverse cleaning due to their incompressible structure [13]. Meanwhile, covalent bonding of the membranes allow the use of strong chemicals due to less sensitivity to re-hydroxylation during the cleaning procedure [14,15]. Even more impressive, hydrophilic characteristics that are naturally found in alumina due to the presence of hydroxyl (OH) groups encourage the adsorption of water and can avoid microorganisms fouling to grow on the alumina surface [4,15].

In protein separation processes, a high degree of efficiency in protein separation and purification is becoming increasingly important. The purpose of protein separation and purification is due to enhancement of purity and stability as well as removal of impurities [16]. Mostly, these applications were widely used in dairy [17], pharmaceutical downstream [18] and food processing [19] industries. The important issue in these applications is protein-membrane interaction that occurred during protein separation and purification processes.
Generally, the adsorption and deposition of proteins on the membrane surfaces were occurred via van der Waals forces, electrostatic attraction, hydrogen bonding and hydrophobic interactions [20–22]. The protein-membrane interactions had significantly affect to the fouling, resolution, and protein stability [23]. Thus, the effectiveness of these membrane applications is strongly dependent on selection of membrane's properties. Furthermore, desired membrane's properties in this case are high selectivity and good surface character.

A good surface characteristic refers to the antifouling and antibacterial capability [4,16]. In the earlier decades, poly(ethylene glycol) (PEG) was used as surface modifier on alumina Anopore™ membranes via grafting technique in order to improve surface hydrophilicity [23]. This approach led to a significant reduction in membrane fouling. Generally, membrane fouling can be reduced by improving the preparation methods and modifying the membrane in order to decrease the interactions between proteins and the membrane surface [14]. Therefore, in order to advance the use of alumina membranes for protein separation and purification, it is necessary to understand the preparation methods and their surface modification methods.

In the last three decades, the fabrication of alumina membranes for new processes and applications has undergone rapid growth in food processing, biotechnology and wastewater treatment [24–27]. Generally, several techniques can be employed to fabricate ceramic membrane such as slip casting [28], extrusion [29] powder pressing [12] and vapour phase deposition [30,31]. Usually, ceramic membranes are fabricated as a multi-layered structure [32] with gradual changes in pore size and thickness from one layer to the other. Recent applications of ceramic membrane have placed it in the limelight of biotechnology due to its efficiency in protein separation and purification and the fact that it fits a certain size range [16].

A number of studies have explored the fabrication of alumina membranes in different configurations such as flat-sheet, tubular, and hollow fibres. Furthermore, alumina membrane also used as a support to produce composite membranes [23–35]. The structure of a membrane can be further modified to enhance permeability and separation factors. Modification of a membrane can be applied to the internal pore surface or on to the top of the membrane to prevent the adsorption of protein which causes fouling [14]. Efforts have been made to improve the membrane surface using a few modification techniques.

There are very limited reviews that describe the surface modification of alumina membrane, while membrane surface modification is an important issue that should be addressed to enhance the efficiency of protein separation and purification. This review mainly focuses on the progress of alumina membrane towards surface modification and its effects on hydrophilicity enhancement and fouling reduction. The discussion provides insights into its potential applications in the field of protein separation and purification. The last part of the review focuses on new findings about modifier materials, especially graphene-derivatives which offer high hydrophilic characteristics. Thus, this review article will provide an extensive reference for researchers working on the recent development of graphene derivative-alumina composites.

2. Overview of alumina membranes

2.1. Characteristics of alumina membranes

Alumina or also known as aluminium oxide (Al₂O₃) is the most common ceramic material used in membrane fabrication owing to properties such as high surface area, resistance to organic solvents, narrow particle size distributions, high density and low fabrication cost [32,36]. Table 1 shows the mechanical and thermal properties of alumina as a ceramic material in membrane fabrication. Moreover, alumina is the most economical ceramic membrane material with regards to its chemical stability in strong acid solvent [12] in comparison with common stainless steel 316. All these characteristics combined with its abundance have made alumina an attractive ceramic material. The selections of raw material powders as well as particle size are important in determining the properties of membrane structure. Commercial alumina ceramics are commonly made of alumina powders with a particle size in the range of 20–40 µm [24].

Physical properties such as pore size and pore size distribution of membrane are the key matters in separation performance [37]. Indeed, particle size distribution is an important material characteristic in the preparation of an asymmetric membrane because it is directly related to pore size and porosity [38]. In order to achieve a good asymmetric structure, different particle sizes alumina is used in fabrication. Kingsbury and Li developed asymmetric hollow fibres using alumina of three different particle sizes [39]. The different particle sizes are fine, medium and coarse, which easily fill in all the spaces of the specimen including tiny spaces, gaps and interior pores. This arrangement leads to a decrease in porosity with an increase in densification, corrosion resistance and asymmetric ceramic membrane strength [40]. In practice, membranes need to be highly permeable, corrosive resistant, have a narrow pore size distribution and perfect surface quality without defects. Thus, among metal oxide materials, alumina is the most promising option in the preparation of ceramic membranes due to its small amount of shrinkage during sintering [41].

2.2. Structure of alumina membranes

Ceramic membranes consist of several thin layers with an overall thickness of between a few nanometres up to a few microns [24]. Alumina membrane applications mostly utilise a porous structure. Porous membranes are widely used in industries that involve solid-liquid and solid-gas separation. This is primarily due to their high structural durability, easy cleaning, low energy consumption and controllable microstructure [44,45]. Porous membrane comprises of a 3-dimensional interconnected network of either symmetric or asymmetric structure [46] as presented in Fig. 1. Symmetric structure refers to pores that are equally sized throughout the membrane while asymmetric structure refers to pore size that gradually decreases towards the surface where separation occurs. Processes of porous membranes are based on the size exclusion of matter in which rejected substances have sizes bigger than the pores of the membranes [47].

Pressure driven membrane processes, that is, microfiltration (MF), ultrafiltration (UF) and nanofiltration (NF) as shown in Fig. 2 are widely used in protein separation application. MF membranes have pore sizes in the range of 0.05–10 µm, which make them able to retain cells and cell debris while allowing proteins to permeate [48]. Meanwhile, UF membranes have pore sizes of 1–100 nm, making them highly desirable for protein separation [16]. Furthermore, their application is also focused on protein concentration such as protein recovery from blood plasma [49] and whey proteins in the dairy industry [50]. On the other hand, NF have pore sizes of 0.5–5 nm that are used to separate solutes based on particle charge and size [16]. Thus, NF ceramic membranes can be applied in the separation of

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Mechanical and thermal properties of alumina [42,43].</th>
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<tbody>
<tr>
<td><strong>Mechanical properties</strong></td>
<td></td>
</tr>
<tr>
<td>Tensile strength (MPa)</td>
<td>117–173</td>
</tr>
<tr>
<td>Bending strength (MPa)</td>
<td>307–413</td>
</tr>
<tr>
<td>Modulus of elasticity (E)×10⁸ (MPa)</td>
<td>21.27–26.8</td>
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<tr>
<td>Compressive strength (MPa)</td>
<td></td>
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<tr>
<td>Modulus of Rigidity (G)×10⁸ (MPa)</td>
<td>1600–3733</td>
</tr>
<tr>
<td>Hardness on the Mohs scale</td>
<td>9</td>
</tr>
<tr>
<td><strong>Thermal properties</strong></td>
<td></td>
</tr>
<tr>
<td>Melting point (°C)</td>
<td>2051 ± 9.7</td>
</tr>
<tr>
<td>Thermal coefficient at 200–1000 °C (°C⁻¹)</td>
<td>8.80×10⁻⁶</td>
</tr>
<tr>
<td>Boiling point (°C)</td>
<td>3530 ± 200</td>
</tr>
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</table>
viruses from the blood stream [48].

2.3. Fabrication methods of alumina membranes

Generally, the fabrication of porous alumina membrane involves suspension preparation, green compact shaping and sintering. Powder, slurry or sol-gel processes can be used for the suspension preparation. The largest concern about the fabrication of alumina membranes is the low cost preparation using two approaches [51]. The first approach is lowering the sintering temperature of the membranes by selecting additives that have a low melting point. The latter approach uses simple fabrication methods such as tape casting [32] and extrusion [32]. The extrusion method is used to produce tubes or multi-channel structures while tape-casting and it is a suitable method to prepare flat sheet structures. Both the extrusion and tape-casting methods require large amounts of organic additives such as binders, plasticisers, and antifoaming agents [53,54]. This leads to the preparation of a homogenous suspension with suitable flow properties in the fabrication process [55]. These additives are removed during the early stages of sintering before the actual densification of the membrane.

Additionally, the most commonly used techniques for the fabrication of ceramic membranes include the pressing [56] and slip casting [57] methods. However, the processing parameters in these fabrication methods need to be clearly understood. The processing parameters consist of characteristics of selected ceramic materials such as particle size and particle size distribution, solid suspension loading, and additive composition [58]. Thus, both methods are suitable for the symmetric structure of ceramic membrane production. Li proposed the preparation of symmetric and composite ceramic as demonstrated in Fig. 3 [59].

Symmetric porous ceramic membranes are produced in two ways, precursor formation and the sol-gel process [60]. In the preparation of precursor formation, various methods can be used such as pressing, extrusion, tape casting and slip casting as mentioned earlier. However, the final membrane products can only be obtained through sintering at high temperature. Meanwhile, multilayer composite membranes can be further processed using the coating technique [61] followed by the sintering, chemical vapour deposition (CVD) or electrochemical vapour deposition (EVD) processes [62]. Usually, multilayer composites have an asymmetric structure which leads to recent applications in protein separation and purification.

The phase-inversion technique is commonly used to produce membranes with asymmetric structures especially for hollow fibre geometry [59]. The process involves slurry-water interface and proceeds into the bulk, thus forming green tape which possesses a two layered structure [63]. The layers are thick, containing large finger-like pores, and thin with no large pores. In practice, fabrication of an asymmetric structure on ceramic membranes was implemented by tape casting using phase-inversion techniques to prepare porous alumina membranes [58]. The resultant green body had the desired flexibility and mechanical strength and was thus easily handled. Therefore, no cracking and wrapping occurred during sintering and alumina ceramic was successfully obtained.

The tape casting with the phase-inversion technique resulted in large finger-like pores in the green tape after removal of the polymer phase through a drying step [64]. Thus, the asymmetric two-layered structure was preserved after the sintering process. The thick upper layer with large pores provided the membrane with sufficient mechanical strength and low mass transport resistance. Meanwhile, the thin lower layer was free of large pores provided the separation process. Furthermore, the phase-inversion technique also resulted in asymmetric ceramics for better permeability [65] and can be directly used in composite membrane formation.

3. Surface modification of alumina membranes

The use of UF alumina membranes has been proven to be an effective process for the removal of natural organic matter and organic macromolecules such as proteins, sugars and humic substances [66–69]. The only problem is the fouling effect during the operation [23]. As contaminants are removed from waste water, they would stay at the surface of the membrane, resulting in cake formation and pore blockage [66]. This phenomenon will cause a fouling effect in the alumina membrane process as well as reduce the separation performance of the membrane process. Thus, the surface character of the alumina membrane needs to be further modified to enhance its anti-fouling properties.

Generally, alumina membranes have a naturally moderate hydro-
Table 2
Preparation techniques of surface modified alumina membranes.

<table>
<thead>
<tr>
<th>Technique</th>
<th>Speed and time</th>
<th>Calined Substrate</th>
<th>Modifier Feature</th>
<th>Application</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coating Dip</td>
<td>0.02 ms⁻¹</td>
<td>1150 °C for 1 h</td>
<td>Martoxide alumina</td>
<td>0.08–0.14 µm (D)</td>
<td>Gas permeation</td>
</tr>
<tr>
<td></td>
<td>20 min at 23 ± 1 °C</td>
<td>–</td>
<td>Dics, 0.41% (P)</td>
<td>Hydrophobic</td>
<td>Protein adsorption</td>
</tr>
<tr>
<td></td>
<td>10 cm/min for 99 s</td>
<td>400 °C for 3 h</td>
<td>Dics, 1150 °C for 1 h Dics, 0.2 µm (S)</td>
<td>TiO₂ sol</td>
<td>Photocatalytic reactor</td>
</tr>
<tr>
<td></td>
<td>1 mm/s for 10 s</td>
<td>350 °C for 4 h</td>
<td>TiO₂ sol 0.2 µm (T)</td>
<td>–5 µm (T), 150.3 nm (S), &amp; 5 µm×5 µm (R)</td>
<td>Fouling study</td>
</tr>
<tr>
<td></td>
<td>10 cm/min</td>
<td>400 °C for 3 h</td>
<td>Dics, 0.2 µm (S), 50 mm (D) &amp; 1 mm (T)</td>
<td>Dics, 0.14% (P)</td>
<td>Martoxide alumina</td>
</tr>
<tr>
<td>Immersion &amp; hydrolysis for 6 h</td>
<td>0.01 ms⁻¹ for 10 s</td>
<td>650 °C for 2 h</td>
<td>Boehmite sol 0.16 µm (T)</td>
<td>Hydrophobic</td>
<td>Protein adsorption</td>
</tr>
<tr>
<td>Immersion for 24 h &amp; hydrolysis for 6 h</td>
<td>20 cm/min for 3 min 30 s</td>
<td>850 °C for 2 h</td>
<td>Tube, 0.4% (P) &amp; 0.2 µm (S)</td>
<td>Hydrophobic</td>
<td>Protein adsorption</td>
</tr>
<tr>
<td></td>
<td>2–5 s</td>
<td>950 °C for 3 h</td>
<td>Tube, 1.4 µm (S)</td>
<td>Hydrophobic</td>
<td>Protein adsorption</td>
</tr>
<tr>
<td></td>
<td>20 cm/min for 3 min 30 s</td>
<td>800 °C for 3 h</td>
<td>Tube, 0.4% (P) &amp; 0.2 µm (S)</td>
<td>Hydrophobic</td>
<td>Protein adsorption</td>
</tr>
<tr>
<td>Immersion &amp; heat at 85 °C for 3 h</td>
<td>2000 rpm for 1 min</td>
<td>65 °C for 10 min</td>
<td>Tube, 0.02 µm (S) &amp; 25–50% (P)</td>
<td>Hydrophobic</td>
<td>Protein adsorption</td>
</tr>
<tr>
<td></td>
<td>1000 rpm/min for 30 s</td>
<td>500 °C for 5 h</td>
<td>Tube, 1.4 µm (S)</td>
<td>Hydrophobic</td>
<td>Protein adsorption</td>
</tr>
<tr>
<td>Spin</td>
<td>350 °C for 4 h</td>
<td>600 °C</td>
<td>Tube, 0.4% (P) &amp; 0.2 µm (S)</td>
<td>Hydrophobic</td>
<td>Protein adsorption</td>
</tr>
<tr>
<td></td>
<td>2400 rpm for 18 s</td>
<td>Disc, 23 mm (D), 0.14 µm (P), 1.44 µm (T)</td>
<td>Hydrophobic</td>
<td>Hydrophobic</td>
<td>Protein adsorption</td>
</tr>
<tr>
<td>Grafting</td>
<td>24 h under nitrogen</td>
<td>100 °C for 12 h</td>
<td>Tubular, 0.2, 0.5 &amp; 0.8 µm (S)</td>
<td>Hydrophobic</td>
<td>Protein adsorption</td>
</tr>
<tr>
<td></td>
<td>Coupling reaction 24 h &amp; ultrasonic 30 min</td>
<td>100 °C for 6 h</td>
<td>Hollow, 42.8% (P) &amp; 0.7 µm (S)</td>
<td>Hydrophobic</td>
<td>Protein adsorption</td>
</tr>
<tr>
<td></td>
<td>Soaking for 12 h</td>
<td>120 °C for 2 h</td>
<td>Disc, 10 µm (S)</td>
<td>Hydrophobic</td>
<td>Protein adsorption</td>
</tr>
<tr>
<td></td>
<td>Immersed for 30 min</td>
<td>120 °C for 3 h</td>
<td>Disc, 3 µm (T) &amp; 30 nm (D)</td>
<td>Hydrophobic</td>
<td>Protein adsorption</td>
</tr>
<tr>
<td></td>
<td>Pour gel into substrate &amp; autoclave</td>
<td>400 °C for 4 h</td>
<td>Tubular, 0.2 µm (S) 30 mm (L)</td>
<td>Hydrophobic</td>
<td>Protein adsorption</td>
</tr>
</tbody>
</table>

*Note: P=porosity, S=size, CA=contact angle, T=thickness, D=diameter, WF=water flux, SR=salt rejection, R=roughness and L=length.
philic character which has a contact angle within the range of 40–50° [70]. The hydrophilic character is known as a water-loving property on a ceramic surface. Hydrophilic membrane features highly polar properties which have the ability to absorb water molecules by forming a hydrogen bond [22]. Indeed, the hydrophilic character retains high surface tension on an alumina surface to repel foulants by reducing adhesion. Meanwhile, strong adhesion between foulants and the membrane surface will cause a fouling effect. Thus, hydrophilic membrane has anti-fouling properties [71]. Anti-fouling properties are important in protein separation and purification. However, alumina membrane is intrinsically hydrophobic due to an oxide material contained in the hydroxyl group. In order to enhance protein separation and purification, a superhydrophilic character of the alumina membrane surface is more preferable.

Although alumina membranes have been widely introduced in protein separation and purification [36], there is still limited study on the fouling effect. Therefore, in order to further advance the use of alumina membranes, it is necessary to understand the chemical and physical phenomena involved. The efficiency of protein separation and purification highly depends on membrane fouling [72]. Membrane fouling may be caused by pore size constriction, pore blockage and a macromolecular aggregate of proteins [4]. All these phenomena will result in membrane fouling by reducing the flux permeation process. Thus, the enhancement of the hydrophilicity of the alumina membrane surface is one of the solutions to remedy membrane fouling.

Currently, researchers focus on two great potentials in surface modification which are superhydrophilicity (contact angle < 5°) and superhydrophobicity (contact angle > 150°) [73]. This attraction is due to the enhancement of its anti-fouling and self-cleaning applications. For instance, Maguire-Boyle and Borron implemented a superhydrophilic surface by coating cystic acid onto an alumina membrane [74]. Cystic acid functionalised alumina coated ceramic to achieve comprehensive wettability when in interaction with water. Additionally, cystic acid contains Zwitter ionic forms which are sulfonil and amine moieties. Numerous hydrogen bonds form between both moieties and solvent during the coating technique. Thus, the superhydrophilic character was performed with increasing permeability and flux of membrane process. Meanwhile, superhydrophilic membranes also can be produced using glass particles as a modified material on a membrane surface [75]. A contact angle of 8° was achieved from a mixture of quartz and glassy additives consisting of zeolite and glass frit. Moreover, the prepared glassy pore wall membrane could stand high thermal and chemical processes.

However, the application of polymer as a modifier material could have drawbacks such as a reduced resistance to high thermal and chemical exposure through industrial applications [75]. To overcome these problems, inorganic materials were selected as the modifier materials due to their properties of high thermal and chemical stability and mechanical strength [76]. Therefore, the application of inorganic materials with nano-size particles as modifier materials was studied in order to enhance their hydrophilic character [77]. For example, nano-TiO₂ particles were used as a hydrophilic modifier on commercial alumina MF membranes [78]. These nanoparticles did not form a separate layer, but increased the hydrophilic character of the membrane surface.

It should be mentioned however, that one of the limiting factors against the application of nanoparticles as modifier materials on a membrane surface is pore clogging [76]. Furthermore, the preparation of a nanoparticle solution also required the sol-gel technique, a high-cost process. Therefore, the selection of modifier materials still needs to be explored for future study in ceramic surface modification.

3.1. Surface modification techniques

Surface modification aims to further decrease the effective pore size and change the chemical nature of the surface [10] resulting in the decline of the fouling effect during the protein separation process [79]. Currently, the study of modification on the alumina membrane is significant, particularly with its focus on the modifier material selection and the development of modification methods. There are two classification methods of surface modification; the chemical method and the physical method [80]. Generally, physical modification comprises of machine-aided approaches such as ion beams, plasma, flame and radiation. The physical method is extensively applied to improve the surface of bone tissue and is widely used in tissue engineering applications [36]. Chemical modification is the direct reaction of certain chemical solutions on the membrane surface. Usually, this method is used to enhance membrane permeability in order to reduce membrane fouling and enhance membrane selectivity [81]. Meanwhile, selected modifier materials could also contribute to the surface modification process via the coating or grafting techniques, thus improving the surface property and fouling resistance of modified membranes.

The preparation techniques and modifier materials used for the surface modification of alumina membranes and the resultant membranes’ features and applications are presented in Table 2. As can be seen, just a few studied was done on surface modification of alumina for protein separation and purification. Meanwhile, various modifier materials and techniques were used to modify the membrane surface. Mostly, focus was given to the modification of alumina membrane by coating with nanoparticle materials [24,76,82] where ceramic membranes were coated with nanoparticles such as sol titania or boehmite in resulting composite membranes. Furthermore, it improved permeability and enhanced the flux [83] as well as the chemical resistance of alumina ceramic in highly acidic and alkaline solutions [51]. On the other hand, composite membranes could also be produced via grafting techniques.

In the case of coating, the coated layer may be easily washed-out during filtration. Meanwhile, the layer produced via the grafting technique is more reliable and durable when applied to modifying the membrane surface, but the method is complicated and time-consuming. Prior to the wide use of coating and grafting techniques, the membrane surface was usually activated by the in-situ hydrolysis technique to introduce an active intermediate interface on the membrane surface [84]. Thus, the application of coating and grafting techniques into the surface modification of alumina membranes will be discussed in more detail in the next sub-section by referring Table 2.

3.1.1. Coating technique

Membrane surfaces can be coated using various coating techniques such as dip coating [100], spin coating [94] and spray coating [101]. In view of its low cost and simplicity, the dip coating technique is the preferred technique in many applications. Membranes for UF and NF can be prepared using the coating process to acquire a small pore size of about 1–100 nm [92]. Meanwhile, coating solution can be obtained using the sol-gel technique to fabricate fine powder [102]. The sol-gel technique is a suspension preparation of small particle-sized materials such as boehmite sol [87], titania sol [49] and ferrooxane nanoparticle [38] as shown in Table 2. Table 2 shows that most researchers studied titanium as the alkoxide precursor in the sol-gel technique for preparing the coating solution. This is because titanium alkoxide is an extremely reactive organic solvent that requires effective control during preparation [49].

The dip coating method is generally used in the development of composite membranes [84,103–105]. Composite membrane usually consists of two or more layers of different materials. For example, alumina-polymer composite contains alumina as support and polymer at the top layer that acts as a penetration and surface covering material [33]. Currently, alumina-polymer composite is widely applied due to its unique combination of properties. The alumina support has high mechanical strength, thermal and chemical stability, while polymer has high selectivity [80]. However, there are two issues in the
preparation of alumina-polymer composite [106]. Firstly, porous alumina requires highly mechanical strength as the support of composite. Second, polymer solution needs to be prepared as a thin layer to enhance membrane permeability. This thin polymer layer reduces the pore size of ceramic, thus offering high selectivity and increased flux [89].

On the other hand, control over the thickness of the polymer layer on the alumina support is a crucial problem [103]. The minimum thickness of the coated layer is offered as maximum in substrate roughness of the membrane [61]. Moreover, the thickness of the composite membranes is influenced by dipping time via dip coating. Falamaki et al., applied the dip coating technique on an alumina MF membrane by focusing on coating time in order to prepare the desired membrane pore size in the range of 0.08–0.14 μm [61]. Meanwhile, an increase in the coating time resulted in more defects on the membrane surface during sintering [22]. In addition, cost and time of preparation of the membrane increased due to the increase in coating time.

Recently, coating materials have become the focus of the study of surface modification on ceramic membranes in order to produce a nano sized coating layer [18]. Nataraj et al. applied cellulose acetate as a polymer coating onto the tubular α-alumina ceramic membrane [89]. The pore size of the resultant membrane was decreased by 10–20 nm from the original pore size of 1.2 μm. Furthermore, cellulose acetate was selected as the coating material due to its advantages such as excellent adhesion to ceramic surfaces, flexibility, commercial feasibility and low cost. Meanwhile, De Angelis and de Cortaleze (2013) used ferroxane nanoparticles as the coating material on the alumina support [38]. As a result, the nanoparticles were distributed homogeneously on the alumina surface with an average pore size of 75 nm. Moreover, the alumina composite demonstrated protein separation with a high selectivity and reduced pore size as well as a reduced fouling effect.

3.1.2. Grafting technique

The grafting technique involved immersion of the alumina membranes in a grafting solution for chemical modification of the membrane surface. Chemical modification occurred by condensation reaction within the reactive group due to the grafting solution and hydroxyl groups on the oxide surface of the membranes [107]. As a result, stable covalent bonds were created between the membrane surface and grafted materials. Mostly, silane groups [96–98] were selected as grafting materials on the surface modification of alumina ceramic as shown in Table 2. Silane groups were reacted with hydroxyl groups on the alumina surface in order to convert the surface character to hydrophobic from its naturally hydrophilic state [107]. According to Hendren et al., the hydrophobic character enhances by increasing the molecular chain length of silane groups in a grafting solution [108]. Hence, the highest length of molecular chain causes more penetration into the pore structure of the membrane surface. These changes of character are applicable for gas separation and oily wastewater treatment [97,109] but not for protein separation and purification processes.

As previously mentioned, the hydrophilic character of the alumina surface is appropriate for reducing the fouling effect during the protein separation and purification processes. Therefore, the grafting technique could also be used to enhance the hydrophilic character of the membrane surface by using hydrophilic grafted materials. This modification used direct monomer grafting onto a ceramic surface. Cao et al., used acrylic acid as the grafting monomer by free-radical graft polymerization on silica membrane [84]. As a result, a ceramic-polymeric pervaporation membrane was prepared with a highly hydrophilic character. To date, researchers are still in search of new grafting materials to enhance the hydrophilicity character of alumina membrane.

4. Recent developments in graphene derivatives on alumina membranes

Nowadays, researchers are looking for new modifier materials which can be applied in surface modification on ceramic membranes such as carbon-based materials. Carbon-based materials such as graphene were explored due to their unique and environmentally friendly properties [110]. Graphene was discovered in 2004 [111] and it consists of a mono-atomic thickness of carbon atoms with a two-dimensional structure. Equally important, it has a large surface area, excellent outstanding chemical resistance and high mechanical properties [112,113]. Furthermore, graphene-based materials could be formed into nano size membranes which exhibit low fictional flow of water [114]. Therefore, the application of graphene derivatives in alumina modification has great potential and needs to be explored in more detail. Two practical methods for preparation of graphene are the chemical and mechanical cleavage methods [115]. The chemical method [116] has been widely applied in the oxidation process of graphite to exfoliate graphite oxide sheets. The reduction process will then form graphene films. As a result, graphene films were successfully achieved in large scale production.

The addition of graphene into alumina powders using the blending technique offered new opportunities in alumina based composite preparation [117–119]. The preparation of a graphene-alumina composite depends on the degree of exfoliation and amount of crystalline defect in the graphene network [120]. Crystalline defect principally differs according to which graphene derivative is used from the selection which includes reduced graphene oxide (rGO), graphene oxide (GO), graphite (Gt) and graphite oxide (GOx) [121,122]. Meanwhile, the dispersion of graphene derivatives in an alumina suspension strongly depend on their van der Waals interactions [116]. Hence, the agglomeration in alumina based composite could cause densification during the sintering process [123]. As a result, using the blending technique to produce alumina-graphene composite is less effective without a detailed mechanism process on alumina-graphene suspensions.

4.1. Challenges in the fabrication of graphene-alumina composites

The fabrication of graphene-alumina composites involves three key issues which are quality of graphene production, homogeneous dispersion of graphene in alumina suspension and retention of graphitic structure during the sintering process [119]. The problem of homogeneous dispersion occurs due to the strong tendency of graphene compounds to agglomerate as a consequence of their inherent hydrophobicity and their high specific surface areas [124]. To overcome this problem, a wet milling process is used on the alumina powders and graphite in ethanol instead of using graphene directly. Exfoliation of the graphite into graphene and uniform mixing of both powders is thus achieved in just one step. However, some graphite agglomerates remained in the suspension and the graphene that is produced is of a low quality. This approach has subsequently been improved using a solution of graphene platelets in dimethylformamide for better dispersion [125]. So far, two main issues have been solved, which are the synthesis of graphene sheets and the preparation of a homogeneous mixture of graphene in an alumina powder [126].

Addressing the issue of graphitic retention structure through the sintering process, researchers are still investigating the use of the Spark Plasma Sintering (SPS) [112,116,119]. SPS is a new sintering technique which is less time consuming due to high heating rates exceeding 300 °C/min compared to conventional sintering. On the other hand, current focus is also being given to other graphene derivatives like graphene oxide on alumina based composite fabrication [126–128].
4.2. Graphene oxide as a noble graphene derivative

Graphene oxide (GO) is a graphene derivative which has a flake-like structure in the micron scale [111]. GO can improve the membrane’s wetting ability due to its high hydrophilic functional group properties. In order to achieve GO structure, graphene surface was modified by attaching water molecules to change its wettability properties from hydrophobic to hydrophilic. GO surface consists of oxygen groups and carboxyl groups which could be suitable for further modification. The oxygen groups can enhance the solubility and dispersion ability of the GO in the ceramic matrix [129]. Meanwhile, the Hummer Method created carboxyl groups on the GO structure due to the oxidation of graphene by strong acids.

The Hummer Method [130] was used to prepare the GO by oxidizing graphite. This method uses a combination of potassium permanganate and sulphuric acid to oxidize graphite. Moreover, GO nanosheets offer an ultrathin, high flux and energy efficient sieving membrane due to their unique two-dimensional, outstanding mechanical strength and good flexibility [131]. Currently, the performance of the GO membrane was focused on the separation of small molecules. This is due to the special structure of the GO membrane which features a high hydrophilic character and less toxicity. It has possible applications in the biological field [129].

However, the structure of GO is still under debate and a popular structural model proposed by Lerf and Klinowski [132] is shown in Fig. 4. GO is mostly composed of carbon and oxygen in atomically thin, plate-like structures. According to this model, several oxygen-containing groups decorate the basal planes (hydroxyl and epoxide groups) and edges (carbonyl and carboxyl groups) of GO [110]. The existence of these oxygen functional groups in GO can be readily dispersed in an aqueous medium and can form well-dispersed aqueous without any addition of surfactants or stabilising agents. In the dispersion of water, GO sheets are highly negatively charged and the result is the ionisation of the carboxyl groups. Moreover, these functional oxygen-containing groups provide many reactive reactions for a variety of surface modification, which can be used to develop a series of functionalised GO-based membranes with significantly enhanced separation performances [133].

4.3. Future prospects on graphene derivatives/alumina membrane

Currently, the application of GO as a graphene derivative on alumina based composite fabrication has earned great attention due to its high permeation and selectivity performance. However, fabrication techniques of GO-alumina membranes still require deep investigation in order to obtain outstanding high permeability with excellent selectivity and stability. The main advantages of GO among other graphene derivatives are highly negative suspension and a high polar character due to the ionisation of the carboxylic acid and phenol hydroxyl groups [110]. The negative charge of the GO sheets provides strong electrostatic repulsion to prevent overlapping among the GO sheets. Meanwhile, the polar character of GO consists of electrostatic and electrostatic forces to allow good dispersion in polar solvents such as water [126]. From experimental measurement, the water contact angles for GO and graphene are 30°–60° and 87–127° respectively [134]. The high hydrophilicity of GO is due to its oxygen-rich groups. Therefore, these factors are in favor with enhancing the water permeability of alumina modified membranes.

Generally, the GO’s reactions are classified into two methods which are reduction (removing oxygen groups) and chemical functionalization (adding other chemical functionalities) [135]. A few applications of graphene derivatives into alumina for composite preparation were shown in Table 3. The dispersion of graphene derivatives in alumina suspension has two methods; either powder or colloidal processing routes. Mostly, researchers have used the powder processing method due to its simplicity and less time consuming preparation [119]. In most cases the suspension is dried and the resulting powder mixture is then compacted by axial pressing. However, the colloidal processing method offers a better quality of dispersion through the surface charges modification of the ceramic and graphene derivative powders [119] resulting in a highly reliable and uniform microstructure.

It can be seen in Table 3 that most of the graphene-alumina composites were tested for a beneficial effect on the enhancement of conductivity [136] and reinforced mechanical properties [123]. The first report on a graphene-alumina composite was published in 2009 [137], where 5% graphite was added to the alumina suspension via the milling process in ethanol at room temperature. The electrical conductivity was found to be 5709 S/m for the composite with a minimum thickness of 3–4 nm. Meanwhile, Lee et al. have reported a strategy to synthesise a GO-alumina mixture using the powder processing method [138], resulting in an increment of up to 21% in the flexural strength. In conclusion, most researchers have tested the graphene-alumina composite for an improvement in mechanical properties such as hardness, fracture toughness and flexural strength.

These enhancements can be significantly improved by loading relatively low graphene derivatives into alumina suspensions. For instance, Centeno et al. reported an improvement of 50% in the fractural strength of graphene reinforced alumina composite with the addition of only 0.22 vol% of GO [127]. However, more recently, GO was used as a grafting material on the alumina surface in order to produce the composite structure as shown in Fig. 5 as reported by Lou et al. (2014). This method uses the silane group 3-Glycidoxypropyltrimethoxysilane (GLYMO) as a linker between the alumina surface and the GO in the Grafting Technique.

However, an important issue is the interfacial adhesion between the separation and support layers [139]. The enhancement of interfacial adhesion is necessary to prevent the membrane layer peeling off from the ceramic surface. Therefore, grafting the GO onto the alumina surface would be a best option in order to enhance its hydrophilicity character of membrane. In protein separation and purification, the high hydrophilic properties would improve the permeate flux and selectivity as well as reduce the fouling effect. Thus, the surface modification of alumina based composite membranes using GO as a
<table>
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<th>Graphene derivatives</th>
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<tr>
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<td>Powders (70 nm)</td>
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<td>Hummers method (1–3 g/L)</td>
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<td>[138]</td>
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<tr>
<td>Hummers method (powders)</td>
<td>Powders</td>
<td>Powder method: sonication &amp; ball milling</td>
<td>1400 °C, 50 MPa with 100 °C/min</td>
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<tr>
<td>Modified Hummers method (Colloid)</td>
<td>Powders (0.2 µm)</td>
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<td>[139]</td>
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</table>
modifier presumably be the future prospect for protein separation and purification. The major future challenge is the mechanism during the surface modification process while attach with GO. Additional research into this mechanism is required in the future development of the GO-Alumina composite.

5. Concluding remarks

In this review, many research works have explained the surface modification of alumina ceramics in order to enhance the separation process. Furthermore, this review also studied the available modification techniques to create alumina membranes with high hydrophilicity thus high performance in protein separation. There are two main approaches to enhance the performance of alumina ceramic membranes to reduce the fouling effect and increase membrane selectivity. Thus, surface modification on alumina ceramic membranes is an attractive technique in order to reduce membrane fouling in protein separation. As a result of this review study, graphene derivatives are viewed as having high potential to serve as modified materials. Future studies are needed to address the issue of hydrophilic character on chemically modified GO sheets. GO sheets as grafted materials and the preparation of an alumina- GO composite are still lacking, mainly due to the performance study of protein separation processes.

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References


