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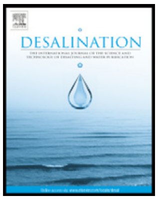

Enantioselective permeation of α-amino acid isomers through polymer membrane containing chiral metal–Schiff base complexes

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ABSTRACT

Herein we report the preparation of thin film composite membranes containing metal complexes with chiral ligands, their characterization and performance evaluation for resolution of racemic amino acids. Schiff base complexes of Cu and Zn metals with chiral ligand were synthesized and cross-linked through amide linkage on polysulfone ultrafiltration membrane by in-situ interfacial polymerization reaction. The membranes were characterized using ATR-FTIR Spectroscopy, Scanning Electron Microscopy and Atomic Forced Microscopy. The permeability and enantiomers selectivity of the membranes were determined in pressure driven process at 1034.64 kPa pressure using aqueous solutions of racemic lysine and arginine as feeds. The effects of permeation process parameters such as, concentration of feed and permeation time, on the performance of membranes were determined. Membranes permeated D-enantiomers of α-amino acids preferentially. Membrane containing Zn complex exhibited better enantioseparation compared to that containing Cu complex. Both of the membranes exhibited higher enantiomeric excess (ee, >94%) for D-lysine.

1. Introduction

Nowadays considerable attention is being paid to chiral chemistry because of significant difference in biological and pharmacological properties of the enantiomers of chiral compounds. One of the paired enantiomers may be active, while other may be inert or even harmful [1,2]. Consequently, it becomes compulsory to evaluate the efficacy of each enantiomer separately. The optical resolution of racemic mixtures is easy and viable method to obtain optically pure enantiomers. The separation of racemic mixtures is possible through various separation techniques, including GC, HPLC, TLC, SFC, etc. [3]. However, these techniques having constraints of being batch processes and can separate only small amount per run and scaling up of process is expensive. The polymer membranes based separation techniques look promising for the separation of racemic mixtures due to their inherent advantages [4]. The polymeric membranes made of different kinds of polymers have been reported for the separation of racemic mixtures. A number of chiral separation membranes were prepared from chiral polymers where enantioselectivity was generated from chiral centers in the main chain. Poly(γ-methyl-L-glutamate) [5–7], alginate [8,9], chitosan [8], cellulose [10] and their derivatives are typically used as chiral polymers for the preparation of chiral separation membranes. Singh et al., develop a method for chiral separation of racemic amino acids using ultrafiltration through immobilized serum albumin membranes, making use of the binding site of bovine serum albumin (BSA) to the L-isomer [11]. Higuchi et al. established that DNA can be used as a biomacromolecular chiral selector in chiral separation technology [12–16]. Majority of polymer membranes mentioned in the literature have been demonstrated the diffusion based separation process wherein driving force for solute transport is concentration gradient across the membrane. The solute flux of diffusion based separation processes is extremely low [17]. The pressure driven separation offers high rate of solute permeability wherein self supported and dimensionally stable membranes are used. The stable polymer membranes based on non-chiral polymer having enantiomers recognizing sites grafted or immobilized indicated loss of enantiomers selective property over a period, therefore such membranes are not acceptable.

Thin film composite membranes exhibiting top thin enantiomers selective property may fulfil the requirements of a suitable membrane for separation of racemic mixtures [18,19]. Earlier we have reported the enantioselective thin film composite membranes for the separation of several α-amino acids [20,21]. Present study focuses on the development of enantiomer selective thin film composite membrane functionalized with Schiff's base metal complexes of chiral ligands. In order to prepare the enantioselective composite membranes, the synthesized chiral Schiff's base complexes of Cu (II) and Zn (II) were incorporated in to the top layer of polysulfone ultrafiltration membrane through in-situ cross-linking with piperazine and trimesoyl chloride. The composite membrane consists of a thin dense top layer and porous support layer. The thin dense layer acts as a barrier or selective layer while the porous layer provides the support for

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the barrier layer. The selective layer of composite membrane is extremely thin (0.1 μm or less) hence permits fast diffusion of solute molecules and thus determines separation efficacy and flux of the membrane. The composite membrane offers excellent combination of selectivity, permeability and mechanical stability [22]. The performance of composite membranes was determined in reverse osmosis mode of separation to achieve high selectivity and permeability.

2. Experimental

2.1. Materials

Racemic lysine, racemic arginine and their optically pure isomers, trimesoyl chloride (TMC) and piperazine were obtained from Sigma-Aldrich (USA). Salicylaldehyde, zinc chloride, copper chloride and other organic solvents were of Analytical Grade purchased from local suppliers.

2.2. Methods

2.2.1. Synthesis of metal Schiff base complexes

Schiff base metal complexes were synthesized by dropwise addition of salicylaldehyde in stoichiometric ratio in methanolic solution of L-lysine and refluxing the mixture at 60 °C for 30 min under continuous stirring. Salicylaldehyde–lysine Schiff base was obtained as bright yellow solid after evaporation of the solvent. 1 mol of salicylaldehyde–lysine Schiff base prepared in previous step was dissolved in 200 mL warm methanol and 1 mol LiOH was added in it slowly. To this reaction mixture 1.2 mol of salicylaldehyde was added dropwise and refluxed for 1 h. A yellow precipitate of disalicylaldehyde–lysine Schiff base obtained which was filtered off, washed with cold isopropyl alcohol and finally dried in vacuum.

2.2.2. Characterization of lysine Schiff bases

Schiff base ligands (SALL and D-SALL) and metal complexes were characterized by elemental analysis (CHNS analyzer, Perkin-Elmer 2400), IR spectroscopy (Perkin-Elmer Spectrum, GX), ^{1}H NMR (Bruker Avance-II spectrophotometer, 500 MHz) and ^{13}C NMR (Bruker Avance-II spectrophotometer, 125 MHz) using DMSO-d_6 as solvent with TMS as an internal reference.

2.2.3. Salicylaldehyde–lysine Schiff base (SALL)

Elemental analysis Salicylaldehyde–lysine Schiff base: molecular formula, $C_{13}H_{18}N_2O_3$ (250.1), calculated values (%): C 62.38, H 7.25, N 11.19. Found (%): C 62.12, H 7.11, N 11.34. IR spectra (Fig. 1a): The presence of C=N stretching at 1465 cm^{-1}, CH_2 absorption at 1451 cm^{-1}, –NH_2 (primary) at 3362 cm^{-1} and –OH (phenolic) at 3143 cm^{-1} confirm the formation of target compound. ^{1}H NMR (DMSO): δ 9.32 (s, 1H), 8.74 (s, 1H), 7.45–7.38 (m, 4H), 7.31–6.76 (m, 3H), 3.55 (t, 2H), 3.50 (s, 1H), 1.7–1.36(m, 4H), 1.87 (t, 2H). ^{13}C NMR (DMSO): δ 177.18 (C=O), 153.92 (C=N), 132.8–115.66 (5 C, phenyl), 63.70 (CH), 60–25.38 (4CH_2).

2.2.4. Disalicylaldehyde–lysine Schiff Base (D-SALL)

Elemental analysis disalicylaldehyde–lysine Schiff base: molecular formula, $C_{20}H_{22}LiN_2O_4$ (361.2), calculated values (%): C 66.48, H 6.14, N 7.75 found (%): C 66.98, H 6.15, N 7.82. IR spectra (Fig. 1b): The presence of C=N stretching at 1469 cm^{-1}, CH_2 absorption at 1449 cm^{-1}, and –OH (phenolic) at 3160 cm^{-1} and disappearance of –NH_2 (primary) peak at 3347 cm^{-1} confirm the formation of D-SALL. ^{1}H NMR (DMSO): δ 10.21 (s, 1H), 8.83 (s, 1H), 8.33 (s, 1H), 7.68–7.57 (m, 4H), 6.79–6.51 (m, 8H), 3.99 (t, 1H), 2.11 (t, 2H), 1.67–1.41 (m, 4H). ^{13}C NMR (DMSO): δ 175.20 (C=O), 162.99 (C=N), 157.00 (C=N), 155.31 (2 C), 123.89–114.76 (10 C, 2phenyl), 69.06 (CH), 61.10–25.39 (4CH_2).

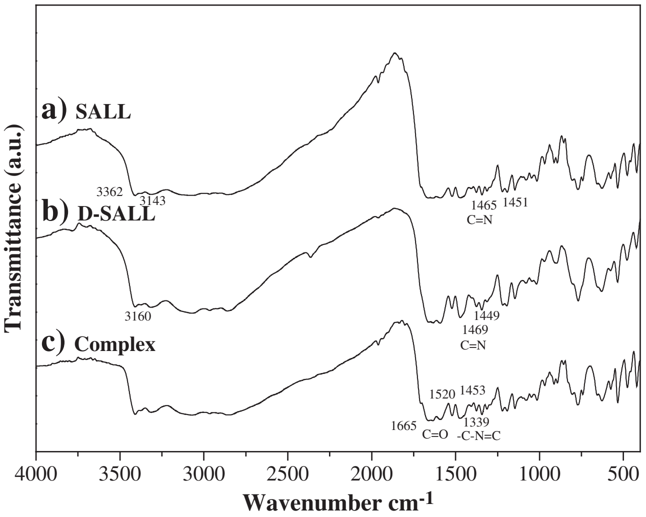

Fig. 1. FTIR spectra of ligands and complex: (A) SALL, (B) D-SALL and (C) Complex.

2.3. Synthesis of metal complexes

The metal complexes were synthesised by dropwise addition of 2 M ethanolic solution of metal chlorides ($ZnCl_2$ or $CuCl_2$) into 1 M ethanolic solution of the disalicylaldehyde–lysine Schiff base, under consistent stirring within 20–25 min at room temperature during which metal Schiff's base complex appeared gradually. The precipitate so obtained was washed with ethanol and dried in vaccum.

2.3.1. Characterization of metal complexes

2.3.1.1. Zn (II) complex. Elemental analysis of complex, Molecular Formula, $C_{20}H_{20}N_2O_4Zn$ (416.1), Calculated values (%): C 57.50, H 4.83, N 6.71 and Zn 15.65, Found (%): C 57.52, H 4.61, N 6.41, Zn 14.80 (by ICP). IR spectra (Fig. 1c): The presence of C=N stretching at 1470 cm^{-1}, C–N=C at 1339 cm^{-1}, CH_2 absorption at 1453 cm^{-1}, C=O at 1665 cm^{-1}, C=C at 1520 cm^{-1} etc. and disappearance of –OH (phenolic) at 3160 cm^{-1} confirm the formation of metal complex. ^{1}H NMR (DMSO) of Zn(II) metal complex: δ 8.65 (s, 1H), 8.32 (s, 1H), 7.40 (s, 1H), 7.40–7.28 (m, 8H), 3.75 (t,1H), 2.59 (t, 2H), 1.73 (t, 2H), 1.78–1.34 (m, 4H) The absence of OH peak at δ 3.12 confirms the formation of metal complex.

2.3.1.2. Cu (II) complex. Elemental analysis of complex, Molecular Formula, $C_{20}H_{20}N_2O_4Cu$ (415.1), Calculated values (%): C 57.75, H 4.85, N 6.74 and Cu 15.28, Found (%): C 57.59, H 4.73, N 6.64, Cu 15.08 (by ICP). IR spectra of Cu(II) complex is near about similar to Zn(II) complex. The presence of C=N stretching at 1473 cm^{-1}, C–N=C at 1341 cm^{-1}, CH_2 absorption at 1458 cm^{-1}, C=O at 1669 cm^{-1}, C=C at 1525 cm^{-1} etc. and disappearance of -OH (phenolic) at 3160 cm^{-1} confirmed the formation of metal complex. Due to paramagnetic complex the resolution is not observed while taking the ^{1}H NMR (DMSO) of Cu (II) metal complex.

2.4. Preparation of composite membrane

2.4.1. Preparation of polysulfone ultrafiltration membrane

Polysulfone ultrafiltration membrane used as support membrane was prepared by phase inversion method. Polysulfone polymer (15 wt.%) was dissolved in N, N-dimethylformamide (DMF) at 60–70 °C under continuous stirring to get homogeneous solution [23]. The polymer solution was evacuated to remove air bubbles and cast on a non-woven polyester fabric 'Nordyl' (Filtration Sciences Corporation,