Iron complexation of pharmaceutical catechin through selective separation

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Supplementary information

Two phase equilibrium study. Extraction and stripping process have been examined primarily in two phase equilibrium studies. .001 M catechin was equilibrated with various stripping solutions and the complexation as well as the precipitation capacities was calculated. The result has been shown in table S1. Ferric nitrate was selected as stripping agent measuring its capacity of complexation with catechin and also precipitation characteristics of the complex.

Transport process. Catechin has been extracted in the present work by the neutral extractant, TBP in the feed side interface of the membrane to form catechin-TBP complex by hydrogen bonding between double bonded 'O' atom of TBP and the 'H' atom of the –OH group of catechin molecule. The complex, so formed, diffuses through the Liquid Membrane (organic phase) to the other side of the membrane to come in contact with the stripping agent (ferric nitrate). The Fe-catechin complex is formed and the carrier TBP is released at the strip side interface (Figure S1). The stoichiometry between metal (ferric nitrate) and catechin in complex was determined employing Job Method (Figure S2). It is assumed that the mass transfer of catechin across the membrane occurs only through diffusion mechanism. The interfacial flux due to the chemical reaction has been neglected, as the chemical reaction is intrinsically very fast, and hence the concentrations at the interfaces will almost be equal to the equilibrium concentrations. The overall flux can be derived by Fick's first law of diffusion applied to the membrane phase (Eq.1).

$$J_{org} = \Delta_{org}^{-1}([CatOH.TBP]_{i,f} - [CatOH.TBP]_{i,r}) \tag{1}$$

Where $[CatOH.TBP]_{i,f}$ and $[CatOH.TBP]_{i,r}$ are the concentrations of catechin-TBP complex at feed-membrane and strip-membrane interfaces, respectively, and Δ_{org} is the resistance to the diffusion of complex in the membrane phase.

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Experimental Section

Chemicals. Synthetic catechin hydrate ($C_{15}H_{14}O_6.H_2O$) was procured from National Chemicals, Vadodara, Gujarat, India. Solvent *n*-decane and carrier tributyl phosphate (TBP) were procured from Merck, Germany. Various metal salts and other reagents were procured from Merck, India. All reagents used in this work were of GR (Guaranteed Reagent) grade. The polymeric membrane (support material) such as polyvinylidene difluoride (PVDF) was procured from Pall Life Science, India. The physical characteristics of the solid support membrane have been shown in Table S2.

Analytical methods. Experimental samples were first centrifuged (Eltek, TC 800 D) in order to obtain a clear solution prior to measurement of concentration of catechin and/or metal-catechin complex in UV-vis. spectrophotometer (Thermo Scientific, Spectrascan UV-2300). Identification of catechin as well as metal-catechin complex was accomplished at appropriate wavelength (279 nm for catechin and a range 190-1100 nm for metal-catechin complex). The others instruments include digital pH meter (Eutech Instruments, pH Tutor) for measuring pH of various samples and the shaking incubator (Daihan Labtech Co. Ltd, LSI 3016R) for two phase equilibrium studies.

Transport experiment. The flat sheet polymeric membrane support was impregnated with membrane liquid (ML) by dipping it in the ML for 24 hours. Solid inert membrane support containing ML into its pores was taken out and the liquid was wiped out gently from the flat surface by good quality non-fibrous tissue. It was fitted in between two flanges connected to feed and strip compartments of experimental set up (Figure S3). The feed phase (130 mL) was aqueous solution of catechin (0.001 M or 300 mg L^{-1}) at pH 5.5. The strip phase (130 mL) was aqueous solution of ferric nitrate of various concentrations. Both aqueous phases were stirred at 200 rpm at 25 ± 2°C using mechanical stirrers (Make: Remi; Model: RGQ 121/D) to reduce concentration polarizations. Before the start of the experiments both aqueous phases were equilibrated with ML. A required amount of electrolyte (NaCl) was dissolved in the aqueous feed phase in order to increase interfacial tension and thereby reduce loss of ML from the pores of the solid membrane. This enhances the stability of LM system. All the transportation experiments were conducted with carrier (TBP) concentration of 1.2 M and this concentration was selected based on the data of past literatures. Vacuum-dried precipitate of metal-catechin complex was weighed and recovery was estimated from the stoichiometry of iron catechin complexation. Feed and strip phase samples (about 3 ml) were periodically taken out and concentration of catechin content in those samples were determined using UV-

vis. spectrophotometer. All experiments were carried out in triplicate and standard deviations were found within ± 4%.
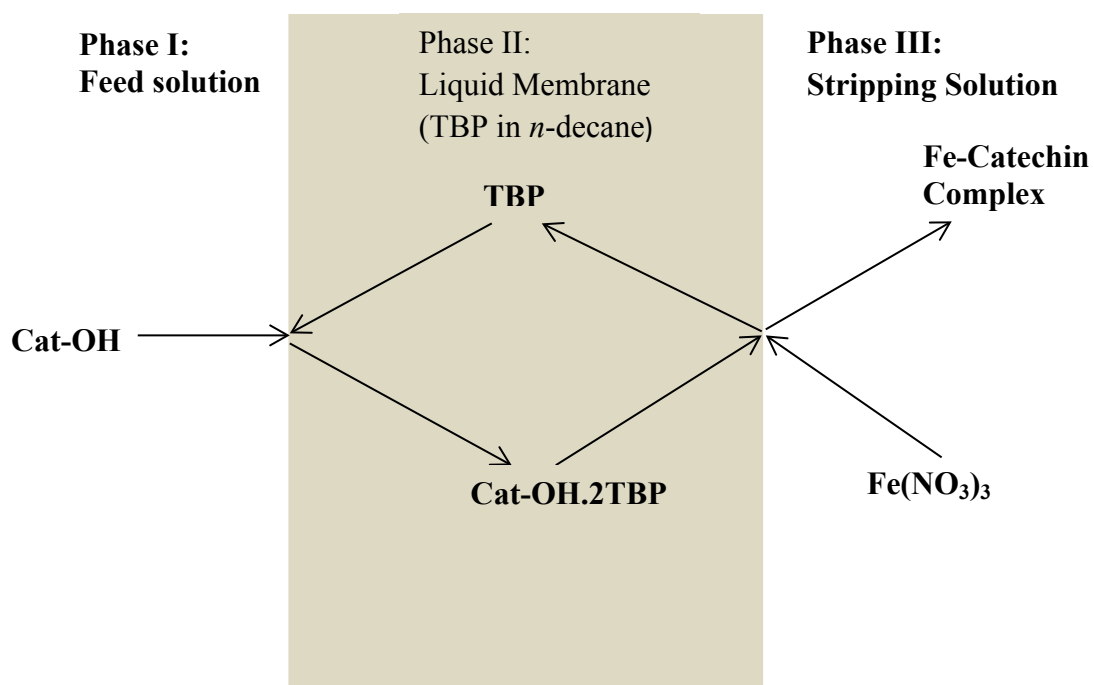
List of Figures

Phase I:
Feed solution

Phase II:
Liquid Membrane
(TBP in *n*-decane)

Phase III:
Stripping Solution

Fe-Catechin
Complex

TBP

Cat-OH

Cat-OH.2TBP

Fe(NO₃)₃

Figure S1. Schematic of the transportation process

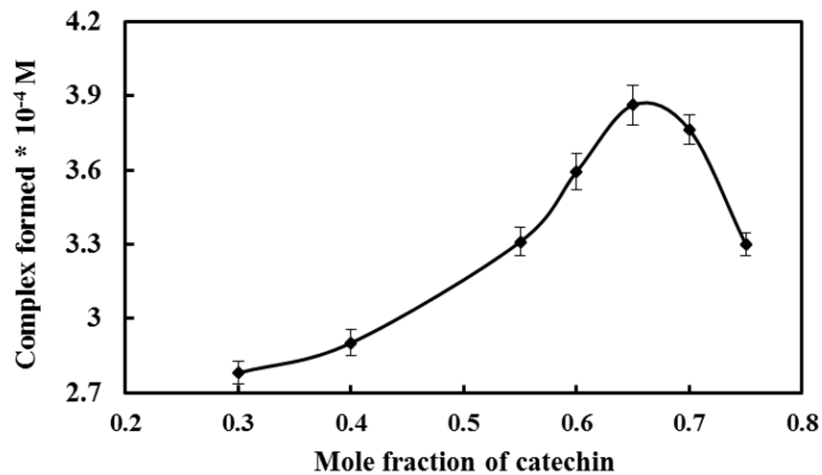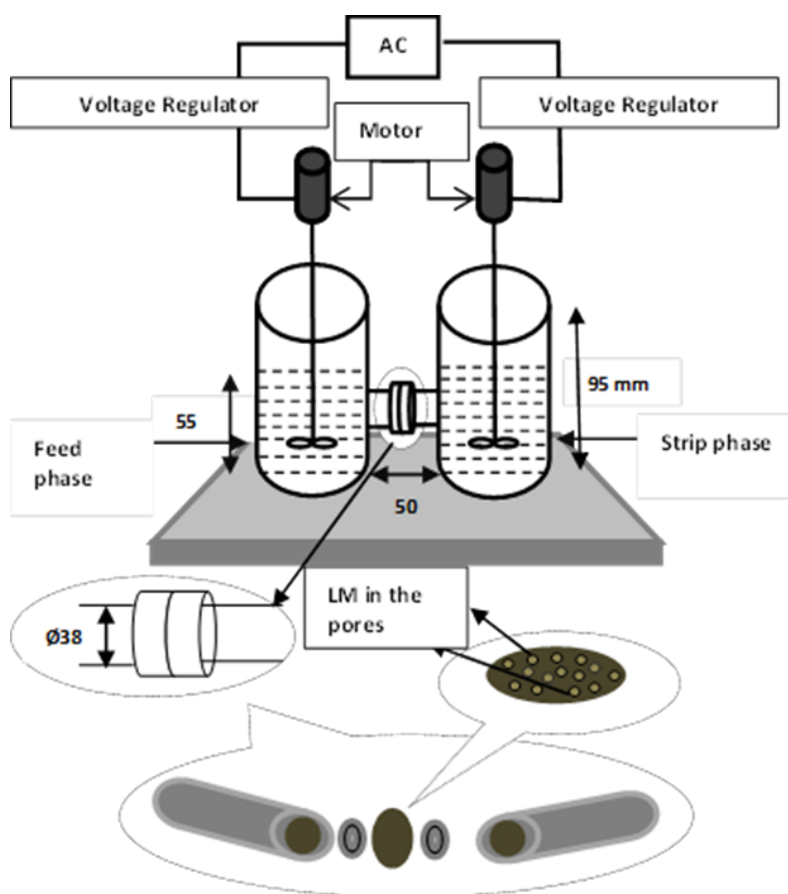**Figure S2.** Reaction stoichiometry of complexation

Figure S3. Schematic of the permeation cell for catechin transportation.

Table S1. Physical characteristics of solid support membrane

Support material	Pore size, d (μm)	Thickness, L (μm)	Porosity (ε)	Tortuosity (τ)
PVDF	0.2	88.5	0.30	5.6

Table S2. Selection of best metal ions to be included in the stripping phase

Metal ions	Standard reduction potential, $E°(V)$[20]	Initial catechin (M)	Unreacted catechin (M)* 10^{-4}	Metal-catechin complex (M)*10^{-4}	%Complexation
Al^{3+}/Al^0	-1.66		4.2	2.9	58
Cu^{2+}/Cu^0	0.34		0.5	4.75	95
Ni^{2+}/Ni^0	-0.25	0.001	1.4	4.3	86
Mg^{2+}/Mg^0	-2.37		6.1	1.95	39
Mn^{2+}/Mn^0	-2.18		4.2	2.9	58
Zn^{+2}/Zn^0	-0.76		2.03	3.98	79.7
Fe^{3+}/Fe^0	-0.04		0.8	4.6	92

Table S3. Calculation of catechin content recovered through precipitation

Component	Molar/atomic weight	One equivalent mole of precipitate (gm)	Precipitate (gm)
Dried precipitate	-	-	0.0309
Molar ratio of catechin to iron (Fe) in the complex = 2:1			
Catechin	290.14	2×290.26 = 580.52	0.0309×580.52/(580.52+58.845)= **0.02806**
Fe	58.57	1×58.845 = 58.845	0.0309×58.845/(580.52+58.845) = 0.00284
Catechin recovered as precipitate = 0.02806 gm			
130 mL of 300 ppm feed solution contains (300×130)/(1000×1000) = 0.039 gm catechin			
Catechin recovered as precipitate = (0.02806×100)/0.039 = 71.95 % ~ 72 % of initial feed.			