Facilitated Transport of Small Carbohydrates through Plasticized Cellulose Triacetate Membranes. Evidence for Fixed-Site Jumping Transport Mechanism

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Facilitated transport through liquid membranes has been investigated for more than 30 years as a potential separations technology.[1] Although liquid membranes have many promising attributes, there has been little industrial application. The major problem is membrane breakdown due to leaching of the membrane components into the aqueous phases.[2,3] Most attempts to overcome this problem have tried to increase the membrane partition ratio by covalently attaching the transport carriers to highly lipophilic or polymeric chains.[4] An alternative approach is to incorporate the transport carriers in plasticized polymeric membranes.[5−10] Although plasticized membranes are used extensively in ion-selective electrodes, they have received only minor attention as materials for separations. The general expectation with plasticized membranes is that the gel-like nature of the membrane increases viscosity which inhibits leaching.[7] On the other hand, the increased viscosity slows diffusion and decreases fluxes for transport systems that use a carrier-diffusion mechanism.[7,8]

This report describes plasticized cellulose triacetate membranes that incorporate a large amount of quaternary ammonium salt as the active transporting component. To date, most of the work has involved plasticized films that are homogeneous mixtures of cellulose triacetate (CTA), plasticizer (*e.g.*, 2-nitrophenyl octyl ether (2-NPOE) or tris(2-butoxyethyl) phosphate (TBEP)) and trioctylmethylammonium chloride (TOMAC).[11] These membranes were recently employed by Hayashita in an anion exchange separation process.[9] They are impermeable to metal cations but allow passage of anionic heavy metal chloride complexes.[10] We now disclose that these plasticized membranes are also remarkably permeable to small, neutral carbohydrates.

The plasticized CTA membranes are prepared using a simple procedure described initially by Sugiura.[9,10] A chloroform solution of CTA (0.10 g), 2-NPOE or TBEP (0.20 g), and TOMAC (0.20 g) is allowed to slowly evaporate in a 9 cm diameter flat-bottomed glass petri dish. The resulting plastic film (50 μm thick) is peeled off, trimmed, and clamped into a cylindrical transport cell that has been described before.[12] Table 1 shows that in the absence of quaternary ammonium salt the lipophilic CTA membranes are nearly impermeable to hydrophilic compounds. However, when the membranes contain a large amount of TOMAC, they become highly permeable to mono- and disaccharides. Moreover, the membranes have good stability and show no evidence of diminished performance after weeks of use.

This remarkable combination of high flux and high stability has prompted us to investigate the saccharide transport mechanism. Two of the most likely mechanistic possibilities are carrier-diffusion and fixed-site jumping.[13] With this latter mechanism, the transporter molecules act as "stepping stones" and the solute moves through the membrane by jumping from one fixed-site to another. The theory of fixed-site jumping has been described by Cussler[13] and Noble;[14] however, very few systems have been characterized experimentally.[13−17] The kinetic profiles for transport by carrier-diffusion and fixed-site jumping are generally quite similar.[18] One major difference is the dependency of flux on transporter concentration. For transport by carrier-diffusion, the expected profile is a linear plot passing through the origin. For fixed-site jumping, a percolation threshold is predicted if transport does not occur when the distance between fixed-sites becomes too great to

Table 1. Noncompetitive Transport Through Cellulose Triacetate Membranes[a]

| entry | plasticizer | transporter | initial flux[b] (10^{-8} mol/(m^2 s)) | | | | |
			glucose	fructose	sucrose	KCl[c]	NaCl[c]
1	2-NPOE	none	1.2	2	0.3	1	1
2	2-NPOE	TOMAC	572	1000	300	<5	<5
3	TBEP	none		15			4
4	TBEP	TOMAC		3180 (3920)[d]			16

[a] Unless otherwise stated both aqueous phases contained sodium phosphate (60 mL, 100 mM, pH 7.3). The source phase also contained saccharide (300 mM). Plasticized membrane (16 cm^2, 50 μm thick) manufactured from CTA (0.10 g), plasticizer (0.20 g), transporter (0.20 g), $T = 298$ K. [b] Flux extrapolated to $t = 0$, reproducibility ±10%. [c] Fluxes determined by change in conductivity. Aqueous phase were not buffered. [d] Flux observed after 1 week of use.

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(5) Plasticized membranes have been referred to in the literature as Solvent Polymeric Membranes,[6] Gelled Liquid Membranes,[7] Polymer Inclusion Membranes,[8] and Polymeric Plasticizer Membranes.[9,10]

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(8) Lamb and co-workers have recently uncovered a carrier-diffusion process that operates in plasticized membranes with high fluxes. Schow, A. J.; Peterson, R. T.; Lamb, J. D. *J. Membr. Sci.* **1996**, *111*, 291−295.

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(10) Sugiura has used plasticized CTA membranes containing quaternary ammonium salts to separate lanthanide ions. Sugiura, M. *Sep. Sci. Technol.* **1993**, *28*, 1453−1463. Sugiura, M.; Hirata, H. *Chem. Express* **1993**, *8*, 249−252. Sugiura, M.; Hirata, H. *Chem. Express* **1993**, *8*, 519−522.

(11) In this study we used Aliquat 336 which is predominately trioctylmethylammonium chloride with a small amount of material containing C$_{10}$ chains. For simplicity, we refer to it as TOMAC. The TOMA salts described in Table 2 were prepared by anion exchange with Aliquat 336.

(12) van Straaten-Nijenhuis, W.; de Jong, F.; Reinhoudt, D. N. *Recl. Trav. Chim. Pays-Bas* **1993**, *112*, 317−324. The transport cell consisted of two identical, water-jacketed cylindrical halves (half-cell volumes of 60 mL, membrane area of 16 cm^2) that were stirred by turbines which in turn were driven by externally situated magnets. The side of the film exposed to the air during the evaporation process was placed facing the source solution. Saccharide concentrations were determined by enzymatic assay of small aliquots.

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(17) (a) Shinkai, S.; Torigoe, K.; Manabe, O.; Kajiyama, T. *J. Am. Chem. Soc.* **1987**, *109*, 4458−4464. (b) Shchori, E.; Jagur-Grodzinski, J. J. *J. Appl. Polym. Sci.* **1976**, *20*, 773−788.

(18) Both mechanisms are expected to produce a flux versus solute concentration curve that tends to an asymptotic flux value at high solute concentrations.[13] We find that a plot of fructose flux versus fructose concentration for a constant TOMAC content (0.1 g) was slightly curved but well short of TOMAC saturation, which is not surprising considering the large amount of TOMAC used.
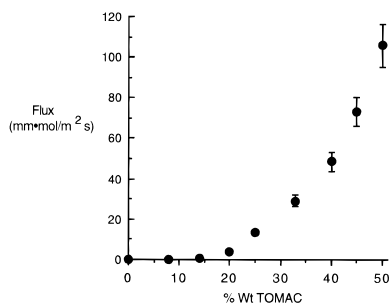
Figure 1. Fructose flux versus % wt of TOMAC in plasticized membranes that also include CTA (0.10 g) and 2-NPOE (0.20 g). Fluxes are adjusted to account for differences in membrane thickness. See Table 1, footnote *a* for other conditions.

Scheme 1. Postulated Fixed-Site Jumping Transport Mechanism
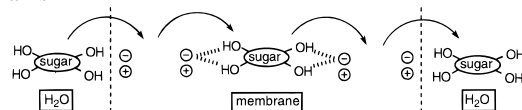
allow solute jumping. Below the threshold concentration, flux is negligible. Above the threshold concentration, flux may vary linearly with transporter concentration or at a higher power, depending on the experimental conditions.[13,14]

Thus, we investigated fructose flux as a function of carrier concentration and found strong evidence for a percolation threshold. Significant transport did not occur until the TOMAC content was greater than 20% of the total membrane weight (Figure 1). A simple calculation indicates that this threshold concentration corresponds to an average distance between TOMAC ion pairs of ~14 Å. This result leads us to postulate a fixed-site jumping mechanism with chloride ion acting as a fixed-site sugar receptor (Scheme 1). Further evidence in favor of this mechanism includes the following:

(1) TOMAC only weakly extracts monosaccharides from aqueous into chloroform solution but it significantly facilitates fructose transport through a polymer-supported liquid membrane (solution of TOMAC in 2-NPOE supported by a thin, flat sheet of microporous Celgard). When the TOMAC content is above 20% wt the TOMAC transport order is about 2, a result that is in agreement with a fixed-site jumping mechanism (see Supporting Information).

(2) There is literature evidence suggesting that TOMAC exists primarily as non-aggregated ion pairs or even free ions in 2-NPOE or TBEP (the dielectric constant for 2-NPOE is 24 which is very similar to that for acetone) and that the chloride hydration number is around 4.[19] Schneider and co-workers recently showed that chloride ion associates with diol-containing compounds in organic solvents.[20]

(3) The CTA membranes absorb a small amount of water (about 2% wt) and remain transparent throughout the transport experiment. On the other hand, analogous plasticized PVC membranes quickly turn opaque (PVC membranes are known to form water clusters[22,23]) and exhibit very low sugar permeabilities. Thus, the CTA is more than an inert polymer support. It is a crucial membrane component that appears to hydrate the membrane in a way that PVC cannot.

(4) If the aqueous phases contain sodium chloride (0.1 M, pH 7.3) instead of sodium phosphate, the fluxes are lowered by an order of magnitude. The reason for this effect is not com-

Table 2. Fructose Transport through Cellulose Triacetate Membranes Containing Different Plasticizers and Transporting Agents[a]

		initial flux[c] (10^{-8} mol/(m² s))	
entry	transporter[b]	NPOE	TBEP
5	none	2	15
6	TOMA chloride	1000	3180
7	TOMA bromide	460	2340
8	TOMA tetraphenylborate	*d*	5
9	TOMA 4-toluenesulfonate	9	163
10	TOMA bis(2-ethylhexyl)-phosphonate	26	123
11	TOMA 4-methylbenzoate	40	590
12	TOMA diphenylphosphinate	105	600
13	tetrahexylammonium chloride	*d*	1260
14	tetrabutylammonium chloride	*d*	40
15	tridodecylmethylammonium chloride	39	*d*
16	tetraoctylphosphonium bromide	42	330

a Table 1, footnote *a*. *b* See ref 11 for definition of TOMA cation. *c* Flux extrapolated to $t = 0$, reproducibility ±10%. *d* Unable to form a plastic membrane.

pletely clear; however, membrane analysis experiments indicate that is not due to leakage of the TOMAC or anion exchange within the membrane. When the aqueous phases contain sodium chloride, a plot of flux versus membrane TOMAC concentration still exhibits the percolation threshold seen in Figure 1.

(5) Monosaccharide transport was recently achieved through bulk, liquid membranes using reverse micelles.[24] However, we find little or no transport through plasticized CTA membranes containing Tween 85 or Span 60; two compounds that are well-known to form reverse-micelles.

(6) Flux is dependent on membrane thickness. Stacking multiple membranes together or preparing a single membrane of additional thickness lowers fructose flux in a linear fashion.

(7) We have initiated a survey of transporter cation and anion effects. The results to date are summarized in Table 2. Interestingly, the relationship between saccharide flux and anion hydrogen-bonding ability is not linear; chloride is the best anion. There also appears to be a significant cation effect, with the more surface active TOMA cation producing the highest flux.[25]

In conclusion, we have discovered a novel class of plasticized cellulose triacetate membranes that are selectively permeable to small carbohydrates. The fluxes are very high, and the membranes have good stability. The evidence to date is consistent with a fixed-site jumping process.[26] A mechanistic model has been proposed that suggests how the process can be improved and made more selective. Our results indicate that facilitated transport through plasticized membranes by fixed-site jumping is an effective way to solve the enduring problem of membrane instability.

Supporting Information Available: Experimental details and results of transport through polymer-supported liquid membranes (2 pages). See any current masthead page for ordering and Internet access instructions.

JA964103M

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(26) Sugar transport through polymeric anion exchange membranes has been studied before. In two cases, the permeation was interpreted as a background leakage effect with no specific interaction between the sugar and the membrane [Igawa, M.; Sekimoto, T.; Okochi, H. *J. Membr. Sci.* **1995**, *98*, 177−180. Ouahid, S.; Métayer, M.; Langevin, D.; Labbé, M. *J. Membr. Sci.* **1996**, *114*, 13−25]. A third case utilized a coupled counter transport mechanism [Shigemasa, Y.; Okamoto, S.; Sahiwa, H.; Saimoto, H. *Chem. Lett.* **1990**, 433−436].