Permeation and Absorption of Ethanol/Water Mixture through Ethylcellulose Film

Jin Zhao*, Daniel Burnett‡, Armando R. Garcia‡, Jason Folkenroth*

*DuPont Nutrition & Biosciences, Midland, MI 48642, USA;

‡Surface Measurement Systems, Allentown, PA 18103 USA

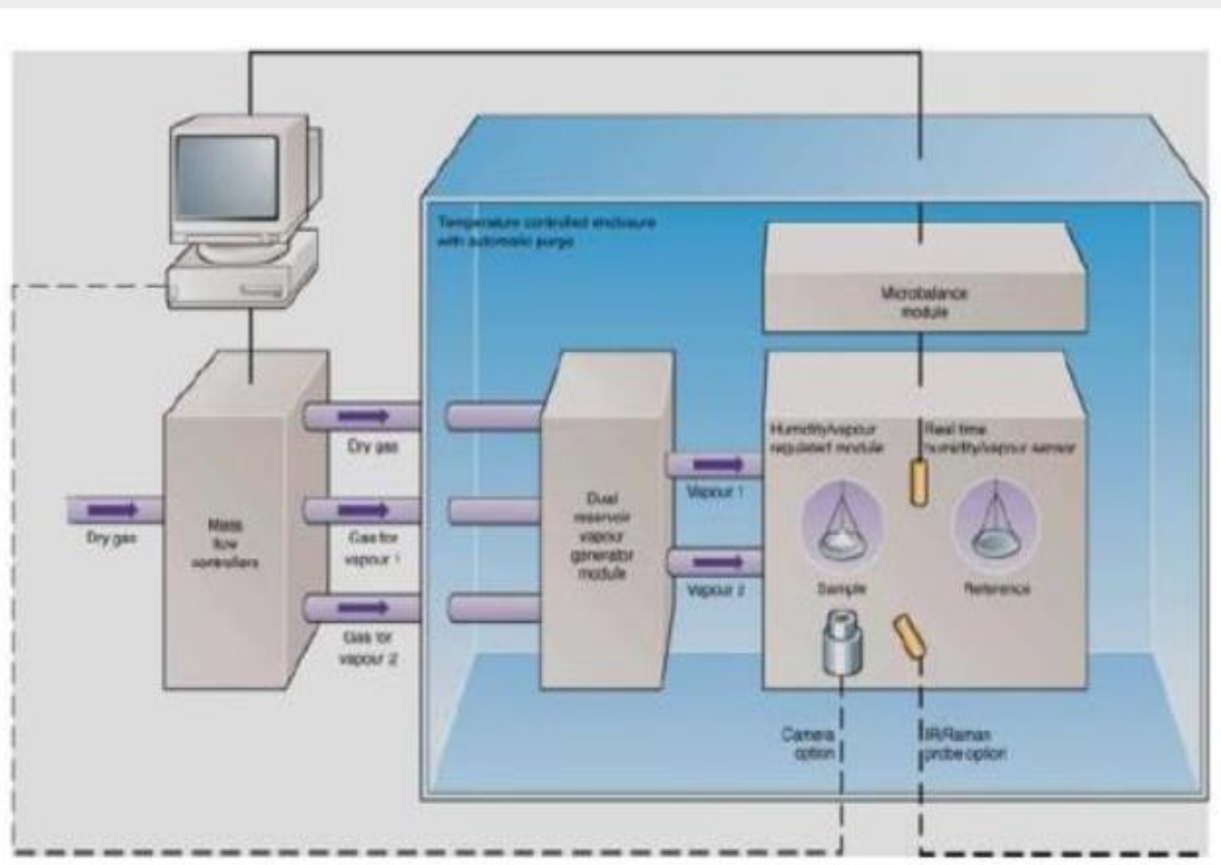
PURPOSE

Ethylcellulose (EC) is water-insoluble, rate-controlling polymer which has been widely used as coatings of oral solid dosage forms, excipients for amorphous solid dispersions of active pharmaceutical ingredients (APIs), and films for buccal and transdermal drug delivery systems. The interaction of alcohol/water mixtures with EC films will ultimatively impact the drug delivery of the dosage form and thus the therapeutic and prophylactic outcome of the actives. The affinity of the spray solvent for EC can also impact drying rate, secondary drying rate (removal of residual solvent in a secondary batch process), and the glass transition temperature of the spray-dried dispersion. This study is to understand the interaction of alcohol/water mixtures with EC films of varying molecular weights which have been cast from organic solutions. These results can help pharmaceutical scientists design coating formulations for protection and/or modifying release of APIs with potential alcohol exposure or ingestion.

METHOD

Films were cast from organic solution of ethylcellulose polymers with viscosities ranging from 21 to 29 cP. Solvent vapor transmission rate (SVTR) and equilibrium solvent content were determined with a Dynamic Vapor Sorption analyzer (DVS-Resolution). Various EC films were analyzed over a relative partial pressure (P/P_0) range of 0-90%. The vapor program began by exposing the sample to dry air to establish the dry mass. Then, the vapor concentration was increased in 10% P/P_0 steps from 0 to 90% P/P_0. The vapor concentration was then decreased in a similar manner to accomplish a full sorption/desorption cycle. Fickian, 1-D diffusion coefficients were determined at each relative partial pressure level.

Figure 1. Dynamic Organic/Water Vapor Sorption (DVS) using DVS resolution.



RESULTS

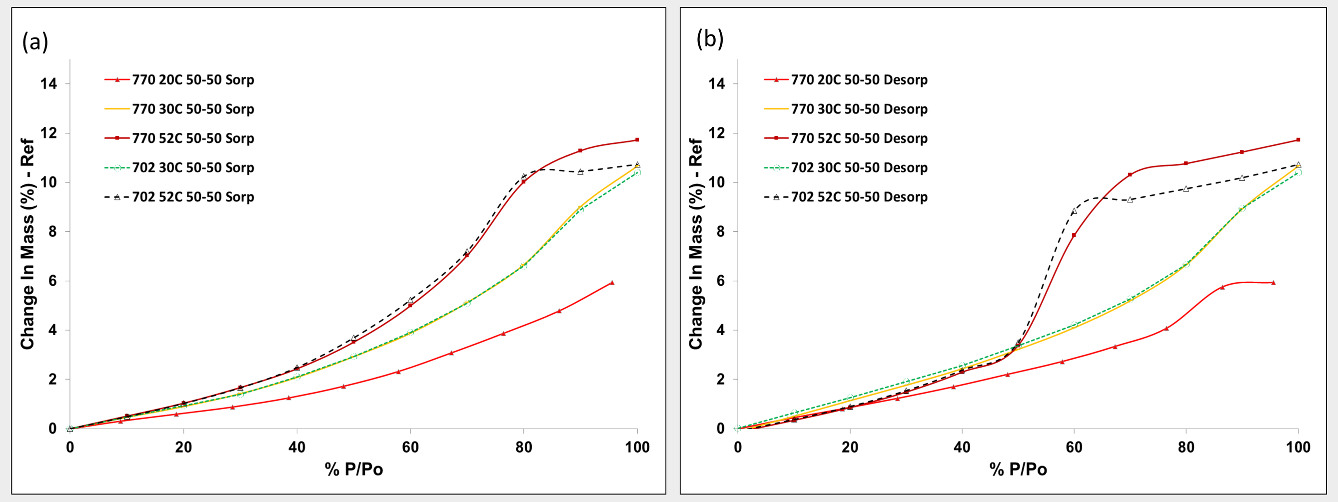
Solvent Sorption/Desorption and Diffusion Behavior of EC Films

Table 1. Key characteristics of EC film samples used in this research.

Sample Name	Viscosity[a], cP	Ethoxyl, %	Casting Solvent
EC film 770	21.3	48.7	Ethanol, 200 proof
EC film 702	28.7	48.9	Ethanol, 200 proof

[a]5% EC in 80/20 toluene/EtOH

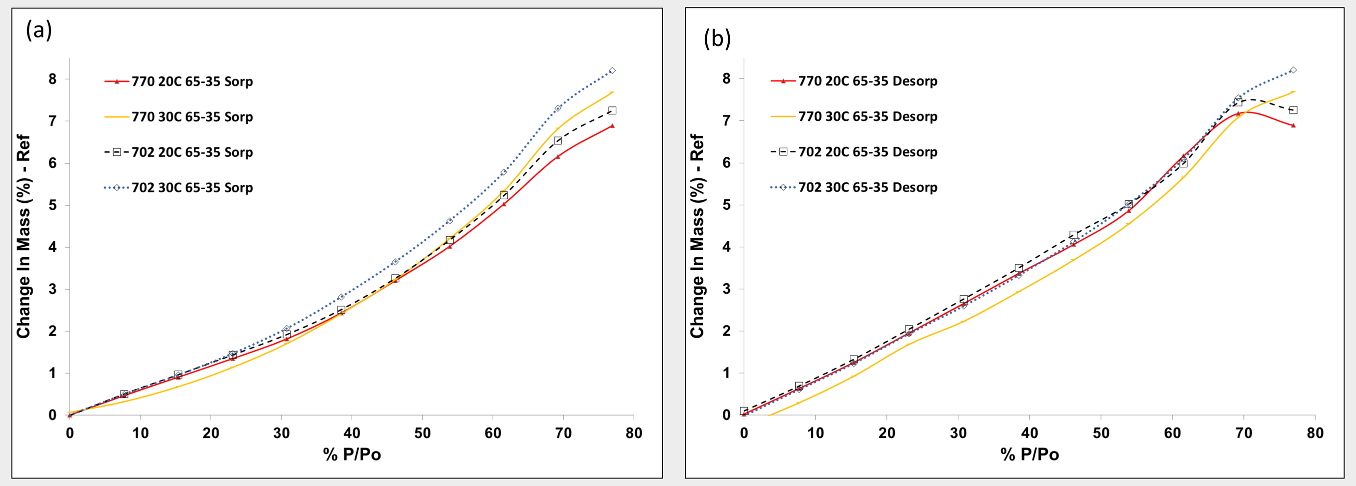
Figure 3. Sorption (a) and desorption (b) of ethanol/water 50/50 (mole ratio) at 20, 30, and 52 °C for EC film 770 and 702.



❖ The total isothermal solvent absorption increased with increasing temperature.

❖ There were only slight difference between EC 702 and EC 770 films when exposed to the 50/50 ethanol/water solvent system at 20, 30, and 52°C.

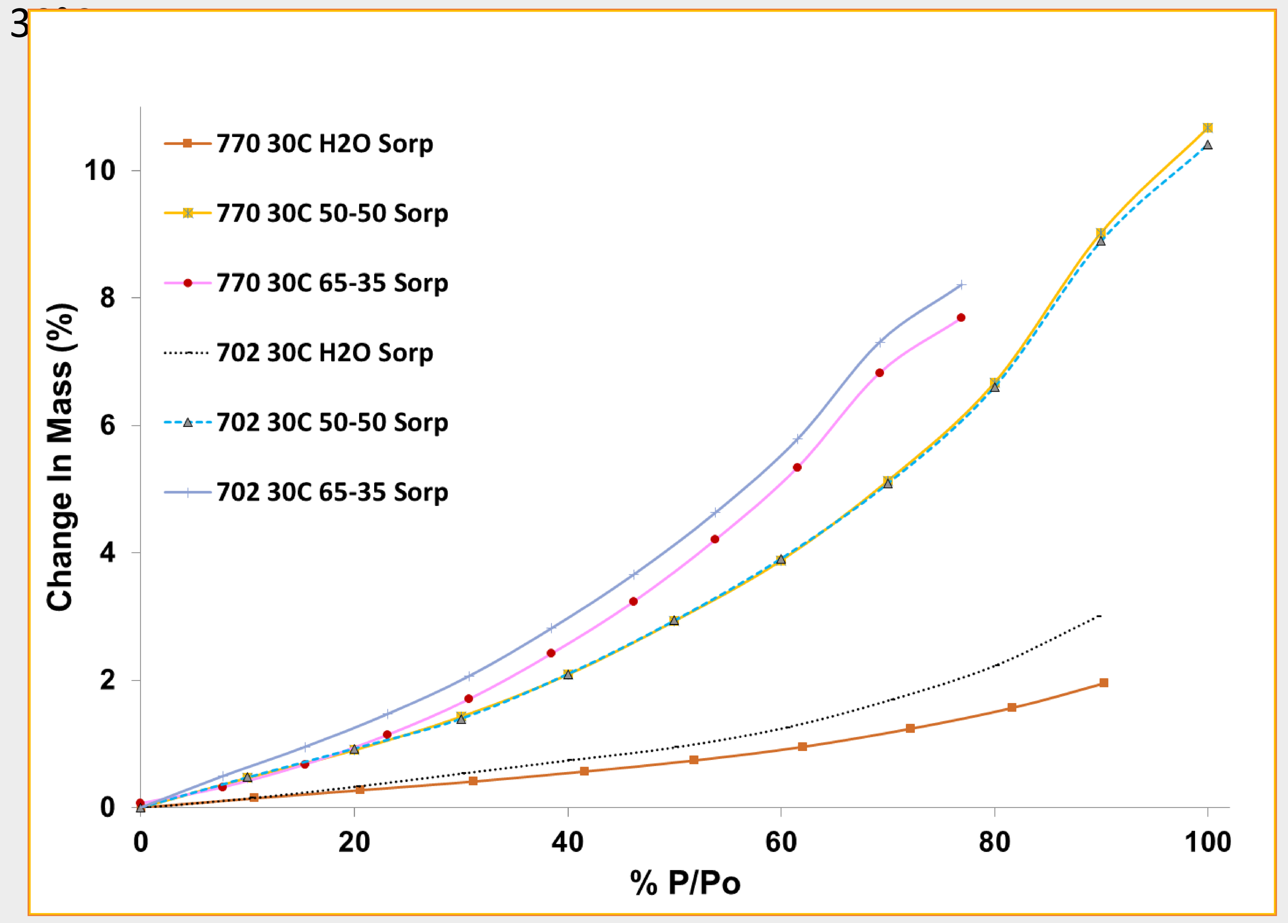
Figure 4. Sorption (a) and desorption (b) of ethanol/water 65/35 (mole ratio) at 20 and 30°C for EC film 770 and 702.



❖ The total solvent absorption isotherm increased with increasing temperature.

❖ There were only slight difference between EC 702 and EC 770 films when exposed to 65/35 ethanol/water solvent system at 20 and 30 °C.

Figure 2. Water/ethanol sorption isotherm of EC film 770 and 702 at 3

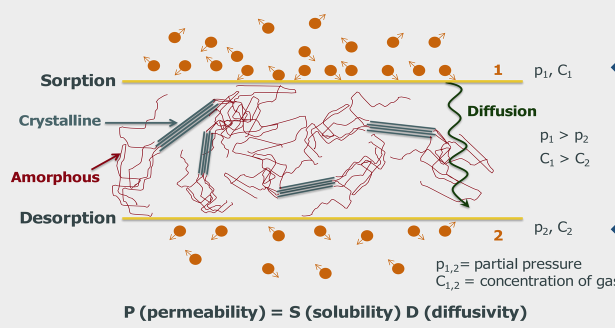


❖ The EC films with higher MW (EC film 702) showed higher water and ethanol absorption at 30 °C than that of lower MW.

❖ There were only slight difference between EC 702 and EC 770 films when exposed to mixed solvent system at 30 °C.

Table 2. Solvent permeation of EC films.

Sample	T, °C	Permeant H_2O, mole %	Permeant EtOH, mole %	P/P_0 (sum), %	$P(H_2O)/P_0(H_2O)$, %	$P(EtOH)/P_0(EtOH)$, %	Permeation Flux, g/m2/hr	Molar average Flux, g/m2/hr
770	30	0	100	50		50	22.1	
770	30	100	0	50	50		4.3	
770	30	50	50	50	25	25	11.2	13.2
770	52	50	50	50	25	25	33.7	
770	52	35	65	50	17.5	32.5	57.7	
702	30	0	100	50		50	27.1	
702	30	100	0	50	50		3.9	
702	30	50	50	50	25	25	8.5	15.5
702	52	50	50	50	25	25	36.6	
702	52	35	65	50	17.5	32.5	76.3	

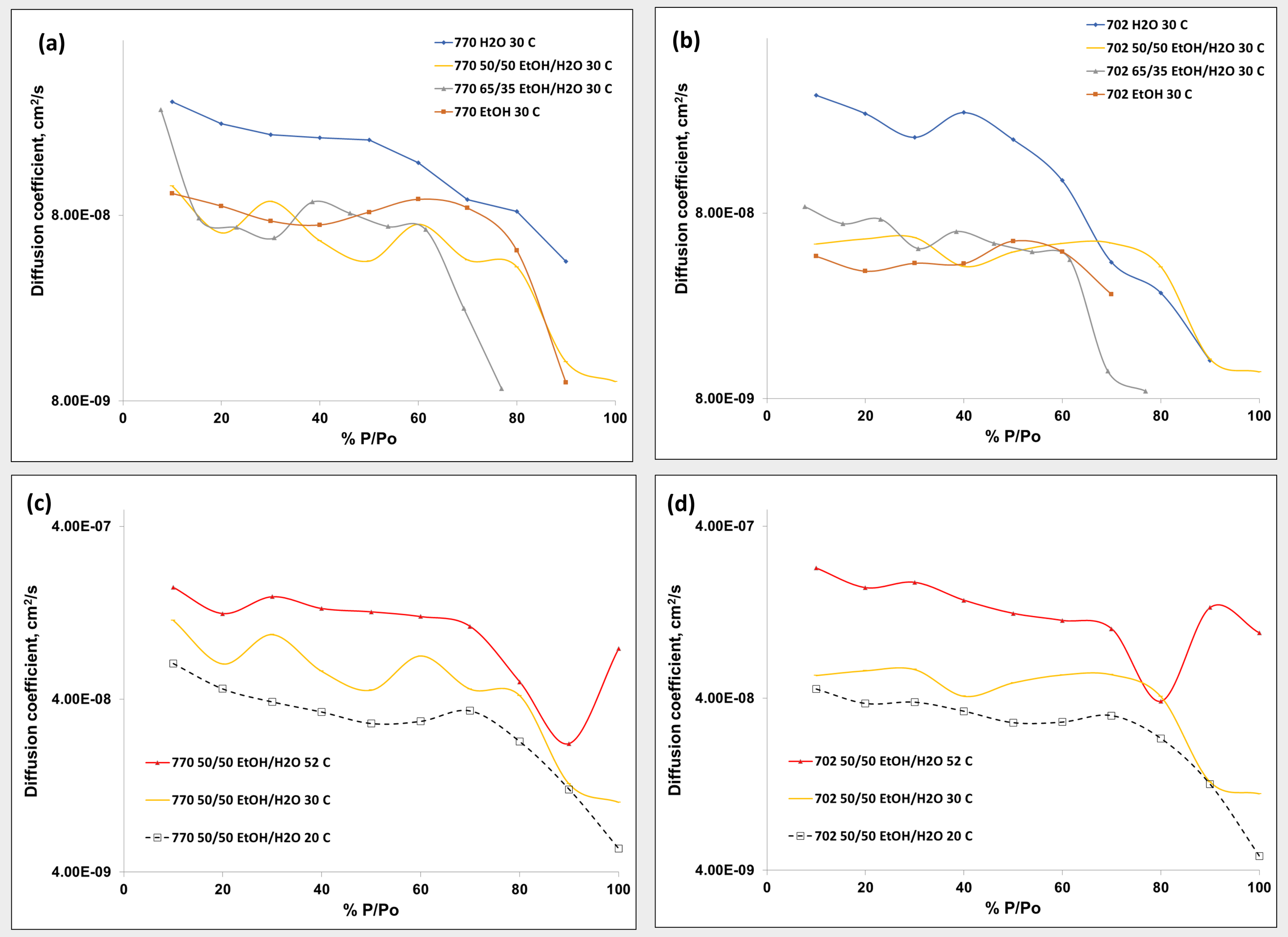


❖ The permeation of EtOH and EtOH/H_2O was higher through EC 702 than through EC 770

❖ The permeation of H_2O through EC 702 was similar to that of EC 770

Kinetics of Solvent Sorption/Desorption in EC Films

Figure 5. Diffusion coefficient of solvent as a function of partial pressure in (a) EC 770 at 30 °C, (b) EC 702 at 30 °C, (c) EC 770 at 20, 30, 52 °C and (d) EC 770 at 20, 30, 52 °C.



❖ Ethanol vapor and ethanol/water vapor has lower diffusion coefficients compared to water vapor

❖ The diffusion coefficients of ethanol/water (50/50) vapor increased with increasing temperature

CONCLUSIONS

Ethylcellulose films serve as a good ethanol/moisture barrier but need to be enhanced when temperatures and/or ethanol concentrations increase. The understanding of the interaction between organic solvent and EC excipients will help formulation scientists design coating formulations that can be used in appropriate protection application for APIs and to improve the spray-dry dispersion process.