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Whilst plasticizers are included in polymer films to prevent embrittlement they may cause modification of solute permeability the extent of which is influenced by plasticizer concentration and leaching from the film (Donbrow & Friedman, 1975). Thus plasticizers may be used to increase control of drug release from polymeric films. In this work two plasticizers differing in hydrophilic properties, have been studied. Films, 19µm[±]0.3µm thick, were prepared by casting acetone solutions of acrylate-methacrylate copolymers A and B (Eudragit RL 100, RS 100, Rohm Pharma, respectively) which differ in quaternary ammonium content in the ratio 2:1, and in one experiment were mixed to give A:B ratios 1.8, 1.6, 1.4, 1.2. Urea permeation was carried out at 30° following Abdel-Aziz & others (1975). Films contained 16.6% w/w total plasticizer obtained by mixing gta and gtb in the proportions shown (Table 1; polymer A) or by using gta alone (Table 2).

Table	1.	Permeability	of	films	with	nlasticizers	of	varving	hydrophilic	character
<u>rubic</u>		reimeubility	01	1 1 1 1110	WIEII	prosererzers		varying	nyarophilite	enarabter

Fraction	of gta		1	0.8	0.6	0.4	0.2	0
	"gtb	1	0	0.2	0.4	0.6	0.8	1
Urea perm	eation rate	e, g.h ⁻¹	0.480	0.480	0.601	0.712	0.803	0.920

gta, glyceryl triacetate; gtb, glyceryl tributyrate

Permeability increased as the content of the more hydrophilic plasticizer gta decreased although the readily leached gta would be expected to increase permeability by providing increased pore space after leaching. However, this effect is apparently overcome as a result of water sorption by the polymer resulting in increased chain flexibility which is contributed to by the more hydrophobic less readily leached gtb which appears to be dominant at high ratios of gtb. Increased water sorption with increasing gtb content can be shown in water swelling experiments.

Table 2.	Effect	of	varying	polymer	cation	content	on	film	permeability
				F /					F

Polymer mixture	А	A1.8	A1.6	A1.4	A1.2	В
Urea permeation rate, g.h ⁻¹	0.480	0.157	0.053	0.035	0.030	0.001

Table 2 reveals a 500 fold decrease in permeability as the polymer mixture changed from wholly A to wholly B. This can be shown to relate to a progressive pore size decrease which reaches 5-fold when B is used alone. Pore formation theory suggests that solid droplets of polymer become joined to form an interconnected structure during separation from a supersaturated solution in which the solid forms the continuous phase and the solvent the disperse phase, (Koenhen &others, 1977); desolvation continues by capillary depletion. Eventual pore size in such a system will be governed by intermolecular attractive and repulsive forces. The lesser repulsive forces in B which contains fewer cationic centres than A will result in the operation of greater cohesive force during film formation culminating in smaller pores which will be associated with lesser hydration capacity and hence correspondingly lower permeability. In the polymer mixtures both components will contribute to overall cohesiveness and the relationship between cohesiveness and pore size may be exploited in the control of permeability.

Abdel-Aziz, S.A.M., Anderson, W. & Armstrong, P.A.M. (1975) J. Appl. Polym. Sci. 19, 1181-1192

Donbrow, M. & Friedman, M. (1975) J. Pharm. Pharmac. 27, 633-646

Koenhen, D.M., Mulder, M.H.V. & Smolders, C.A. (1977) J. Appl. Polym. Sci. 21, 199-215