J. Pharm. Pharmacol. 1998, 50 (Supplement): 182

The effect of collagen solutions on drug release rate from liposomes

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An approach to use of liposomes (phospholipid bilayer vesicles) as a sustained release drug delivery system, should focus on stabilizing the liposomal membrane. Recently, gel matrices or solutions of collagen attracted much attention for this purpose. In this study we tested the effect of collagen solutions (COLLAPUR=COL & COLLAPURON DAK= CD, from Iran Henkle, Representative of Henkle, Tehran, Iran) on the release rate of K2CrO4 (Merck) as a water soluble substance from Stable PluriLamelar Vesicles (SPLVs).

Solutions of COL (0.1,0.3,0.5% v/v) and CD (0.1% v/v) were prepared in distilled water (D.W) with PH=5.5. SPLVs with Diethyl ether and Chloroform (1:1 v/v) as organic solvent, OVOTIN 160 (EPC~ 60%) as the structural lipid and chromate solution in D.W (0.5 &1 M) as the aqueous phase were prepared as previously described (Gruner et al. 1985). One ml of liposome preparation was dialysed with D9997 membrane (from Sigma), then mixed with 3 ml of collagen solutions (for test samples) and D.W (for blank). These preparations were refrigerated under nitrogen for 24 hours. The encapsulation efficiency (EF%) and captured volume (C.V) were then measured using spectrophotometry at 380 nm. Frans diffusion cell, with liposomes (loaded in collagen solutions) as donor, D.W as acceptor phase and D9997 as membrane, was used to evaluate the release pattern at 32°C.

Inspite of previous observations of an increase in encapsulation parameters on reduction of ionic sterengh (Szoka and Papahadjopoulos 1978), it was observed that encapsulation parameters were low (EF%=33.03 0.95 &C.V=30.03 0.86). It is suggested that due to the low ion content of D.W, there is no osmotic gradiant towards inside of liposomes, thus decreasing the encapsulation parameters.

It is reported that type 1 collagen (insoluble form) interacts with liposomes, stabilizes liposomal membrane and reduces the release rate (Pajean et al. 1991). However, in this study the soluble collagens (COL and CD) increased the release rate from liposomes. It is suggested that soluble collagens bind to the surface of phospholipid vesicles, penetrate into the bilayer structure and cause expansion and increasing the permeability of membrane. An increase in release rate in COL (0.1%) and CD (0.1%) in comparison to the blank was observed.

In COLLAPUR solutions (0.3 and 0.5%), the increasing effect of soluble collagens on permeability, is speculated to be compensated by high viscosity. Therefore, the release rate of chromate from these formulations is slow. The release rate of chromate from liposomes does not depend on its primary concentration used to produce liposomes, which confirms that passing of the drug through liposomal membrane is the only limiting step for the release.

It is concluded that using different types of collagens (soluble or insoluble) in appropriate amounts in liposomal formulations could produce a decreasing effect on the release rate, in addition to the dermatological effects of the collagen itself.

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