Scientia Iranica, Vol. 7, No. 2, pp 143–146

SCIENTIA
IRANICA

Research Note

Polymeric Reservoirs for Controlled Release of Iodine in Drinking Water

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In this paper, different polymers are utilized for controlling the release rate of iodine in drinking water to counteract iodine deficiency. Polyethylene, polyvinyl chloride and ethylene vinyl acetate copolymer are used to fabricate polymeric reservoirs of NaI. Zero-order release kinetics with different release rates has been achieved through choosing different materials and various formulation factors. The experimental results are consistent with the expectation that by using a polymer with a greater permeability or a device with a large release area, higher release rate could be achieved.

INTRODUCTION

Iodine Deficiency Disorder (IDD) is one of the most important problems in the world. One billion people around the globe are in danger of IDD with the distribution of: 710 million in Asia, 227 million in Africa, 60 million in Latin America, and 20-30 million in Europe [1]. Twenty million people in Iran are also in danger of IDD [2], which causes goiter, hypothyroidism, cretinism, myxedematous cretinism, barrenness, abortion, etc.

So far, several methods have been used to counteract IDD in different countries. These methods are salt iodination, distribution of iodine tablets, oil or solution and iodine incorporation in drinking water. Degradation of iodine compound in salt and the harmful effects of salt for some people (e.g., those who have high blood pressure or kidney problems, etc.) are drawbacks of the salt iodination method [3].

Previously, silicon rubber compositions and degradable polyesters were used for controlled release of iodine in drinking water [4-9]. In this study, reservoirs of polyethylene (PE), polyvinyl chloride (PVC) and ethylene vinyl acetate copolymer (EVAc) are utilized to deliver iodine in drinking water. Using NaI as the drug, its permeability through these polymers is determined. Considering the amount of drinking water and required iodine for each person, the concentration of iodine in drinking water can be calculated. Then, with respect to the water reservoir capacity, the drug release rate can be determined. Polymeric reservoir can be designed based on the drug release rate, the permeation data and the mathematical modeling. Reservoirs from different polymers are fabricated and the drug release kinetics is studied.

MATERIALS AND METHODS

Materials

Ethylene vinyl acetate copolymer containing 28% vinyl acetate was obtained from Dupont Canada Inc. Polyethylene (high density, melt index = 4 g/10 min) and polyvinyl chloride (Mw = 85000) were purchased from Aldrich Chemical Co. NaI, HCl (90%), toluene, chloroform, 1-2 dichlorobenzene and KIO_3 were reagent grade and obtained from Merck, F.R.G.

Assay Method

Sodium Iodine was used as an iodine salt to counteract iodine deficiency. To assay iodine, a titration method was applied [10]. Based on the following reaction:

$$IO_3^- + 2I_2 + 10Cl^- \rightarrow 5ICl_2 + 3H_2O,$$

10 ml of each sample was mixed with 15 ml HCl (90%) and 5 ml toluene. The concentration of iodine in

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the resultant mixture was determined through titration with KIO_3 solution until the purple color disappeared.

Membrane Fabrication

The solvent casting method was applied to prepare several membranes of EVAc and PVC. Chloroform and 1-2 dichlorobenzene were used as the solvent for EVAc and PVC, respectively. The melting-press machine was used to prepare PE membranes.

Permeation Studies

Diffusion cells containing two equal compartments were employed to obtain the permeability data. The polymeric membrane to be studied was fixed between the two compartments; one compartment (donor cell) was filled with the NaI solution and the other (receptor cell) with distilled water. The initial concentration of NaI in the donor cell was 35 g/l. The containers in each compartment were stirred at a constant rate (750 rpm) to reduce the boundary layer effects. Since the solute diffuses through the membrane from the donor cell to the receptor cell, the concentration in the donor cell decreases and vice-versa. The concentrations of the samples, taken from the receptor cell at three-hour intervals, were measured through titration with KIO_3. Considering the mass balance, the concentration of the active agent in the donor cell was calculated. The plot of $\ln[(C_1 - C_2)/C_i]$ would be linear with a slope of $-2SDK/LV$, where C_1 and C_2 are the concentration of the active agent in the donor and receptor cells, respectively, C_i is the initial concentration of the active agent in the donor cell, S is the membrane area, V is the volume of liquid in each cell, L is the membrane thickness and DK is the permeability of the active agent through the membrane.

Release Studies

To minimize the effect of release from the sides, the peripheral sides were sealed using the following procedure. Glass tubes with 9.8 mm and 17.5 mm diameters were cut into lengths of 2 cm. A film of polymer was fitted into one end of the tube and the tube was filled with the NaI powder. Then, a polymer film similar to the first end was fitted to another end of the tube.

Table 1. Results of permeation of NaI through different polymeric membranes (± means 95% confidence interval for the slope).

Polymer	Permeability $*10^8$ (cm^2/s)
PE	1.18 ± 0.04
EVAc	4.43 ± 0.06
PVC	7.71 ± 0.1

Table 2. Mechanical properties of different polymers.

Polymer	Elongation at the Break	Yield Point Stress (N/cm^2)
PE	6.7	2250
EVAc	> 10	> 1120
PVC	1.05	20000

Immediately after fabricating, the device was put into a beaker filled with 80 ml distilled water. Therefore, the release area would only be the top and bottom of a cylinder. Since visual observation indicated that at 650 rpm, the entire liquid was agitated, the container was stirred at a constant rate (750 rpm) using a stirrer to reduce the boundary layer effects. At 24-hour intervals, the liquid was replaced with fresh distilled water. The concentration of each sample was determined through titration with KIO_3.

RESULTS AND DISCUSSION

The results of the permeation studies of three membranes of each polymer are given in Table 1. The permeability of NaI through EVAc was higher than that through PE and smaller than that through PVC.

To test the mechanical properties, the yield point stress and the elongation at the break for each polymer were determined using the stress-strain profile based on the standard method of ASTM number D882-83 (Table 2). These results indicate that all of the selected polymers possess good mechanical properties.

The release rate profile of NaI versus time over three weeks from the device with the EVAc membrane is shown in Figure 1. The diameter of the glass tube was 9.8 mm, so the release area was $2*75.5$ mm^2 and the thickness of the membrane was 124 μm. The kinetics of drug release from a membrane-reservoir system consists of two parts; transition and steady state condition. Un-

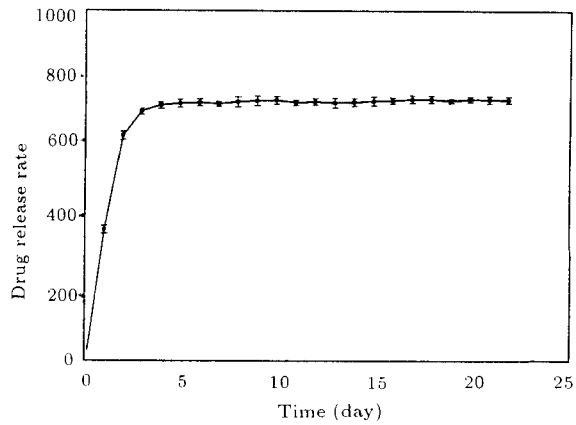

Figure 1. The release rate of NaI from the device with the EVAc membrane (n = 3, error bars represent standard deviations).

der the steady state condition, a membrane device can maintain a constant thermodynamic activity gradient across the membrane for an extended period of time. As a result, a constant release rate, sometimes referred to as "zero-order-release", of the drug is established. A useful equation in describing the release kinetics from a membrane reservoir system with a planar geometry is [11]:

$$\frac{dM_t}{dt} = \frac{2SCDK}{L}, \qquad (1)$$

where dM_t/dt is the drug release rate and C is the drug solubility in water. Prior to the establishment of the steady state, the membrane reservoir device will exhibit initial release rate higher or lower than the steady state value, depending on the previous history of the device. When the device is stored for some time before use, drug will saturate the membrane and, subsequently, give rise to an initial release rate higher than the steady state value. When the device is used immediately after fabrication, a finite time period will be required to establish the steady state concentration profile within the membrane. The transition time for the EVAc device was 5 days. At the steady state, the drug release rate from the device with the EVAc membrane was about 760 ± 5 mg/day, where '$\pm$' means the standard deviation of average measurements of three devices from the time average. Considering permeation results, the predicted release rate, based on Equation 1, is 833 mg/day. The deviation percentage of the predicted release rate from the experimental result was 9.6%.

The release rate profile of NaI over two weeks from the device with the PVC membrane is shown in Figure 2. The release area was 2*75.5 mm^2 and the thickness of the membrane was 300 μm. After the first day of the release, the steady state condition was achieved. The steady state drug release rate from the device with the PVC membrane was about 566 ± 6 mg/day. The deviation percentage of the predicted release rate (599 mg/day) from the experimental result was 5.8%.

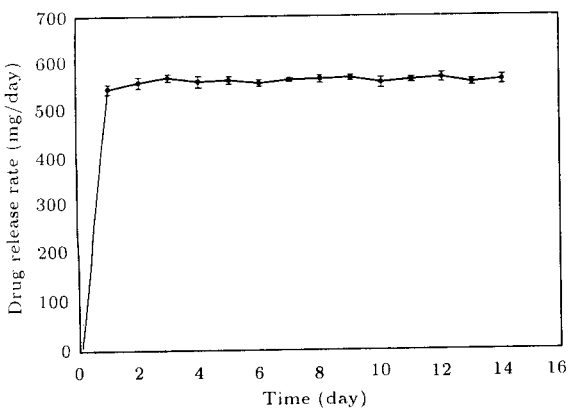

Figure 2. The release rate of NaI from the device with the PVC membrane ($n = 3$, error bars represent standard deviations).

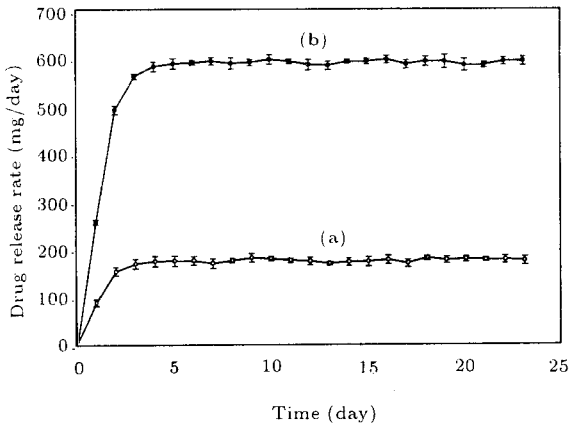

Figure 3. Release rates of NaI from devices with the PE membrane with different release areas (S); a) S = 2*75.5 mm^2, b) S = 2*240.5 mm^2 ($n = 3$, error bars represent standard deviations).

The effects of release area on the drug release rate from devices with the PE membrane have been studied. The release rate profiles of NaI versus time over a three week period for two devices with different release areas are illustrated in Figure 3. The thickness of both membranes was 150 μm. The glass tube diameters were 9.8 mm and 17.5 mm, so the release areas were 2*75.5 mm^2 and 2*240.5 mm^2, respectively. The drug release rate under the steady state condition from the device with the smaller area was 172 ± 6 mg/day, which deviated 6.5% from the predicted value. The steady state drug release rate from the device with the larger area was about 588 ± 8 mg/day which deviated 0.2% from the predicted value. These results are consistent with the expectation that release area is directly proportional to release rate.

CONCLUSIONS

Reservoirs of PE, PVC and EVAc can be used for controlled release of iodine into drinking water. Zero-order release kinetics with different release rates can be achieved by choosing different materials and various formulation factors. The permeability of NaI through EVAc is higher than that through PE and smaller than that through PVC. The experimental results are consistent with the expectation that by using a polymer with a larger permeability, higher release rate could be achieved. On the other hand, as release area increases, so does the release rate of drug. The results of release rate experiments are in agreement with the mathematical predictions.

ACKNOWLEDGMENT

The authors wish to express their gratitude to Drs. M. Barikani and M. Nekoomanesh in the Polymer Research Center of Iran for their kind assistance. The authors also gratefully acknowledge the financial support of Sharif University of Technology Research Council.

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