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Note

Iodine-polyurethane matrices: antimicrobial activity vs method of preparation

E. Touitou [a,1], J. Deutsch [b,1] and S. Matar [a,b]

[a] *Pharmacy Dept and* [b] *Pharmaceutical Chemistry Dept, School of Pharmacy, Hebrew University of Jerusalem, POB 12065, Jerusalem 91120 (Israel)*

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Summary

Polyurethane matrices were prepared by incorporation of iodine during polyurethane polymerization and by immersion of the preformed polymer in iodine solutions. Examination of the IR spectrum has shown that treatment of the polymer with a concentrated solution of iodine produced structural changes in the polymer. Iodine caused a shift of the N-H stretching band to a lower frequency due to the formation of a complex within an intramolecular hydrogen bonding which takes place between the lone pair electrons of iodine and amine hydrogen. The antimicrobial activity was determined by antimicrobial assay according to the European Pharmacopoeia. The results have shown that, for the same concentration of iodine in the polyurethane matrix, a different antimicrobial activity is obtained by using the two different methods of preparation. In patches prepared by the incorporation method, the iodine was strongly bound to polyurethane. In this case, antimicrobial activity was lower than with patches prepared by the immersion method where all iodine was available for antimicrobial activity.

Iodine solutions have long been used as an effective local antiseptic. Due to its high germicidal efficacy and low cost, iodine is still among the most valuable antiseptic agents available. However, iodine is a corrosive substance, and the traditional liquid preparations are known to cause damage to the skin. Free iodine is highly volatile, and generates vapors that are irritating and sensitizing to the eyes, mucosa, and skin. In addition, non-complexed iodine in solution is rapidly inactivated during application. By combining iodine with detergents, solubilizers, or polymers, these problems have been diminished. Such preparations, called iodophores, retain iodine in a loose chemical combination, which also retains bactericidal activity (Lawrence and Block, 1968; Martindale, 1978). However, common iodophores leave carrier residues on the skin. In a previous work, we used commercial polyurethane sheets, Synthaderm®, as carriers for iodine delivery (Touitou and Friedman, 1984). The release profiles of iodine in vitro have been found to be highly sensitive to changes in the device rotational speed: at high rotational speeds the matrix diffusion mechanism controlled the system while at lower rates of rotation the drug was released following a zero-order process. Under conditions of low rotational speed, the major barrier for drug release was found to reside in a boundary diffusion layer.

In the present work, the effect of the method of iodine incorporation on the matrix properties

Correspondence to: E. Touitou, Department of Pharmacy, School of Pharmacy, Hebrew University of Jerusalem, Jerusalem, P.O.Box 12065, Israel.
[1] Affiliated with D.R. Bloom Center for Pharmacy.

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of iodine-polyurethane delivery systems prepared by two different methods was investigated.

Hypol foamable hydrophilic prepolymer (FHP) 2002P was obtained from W.R. Grace and Co. (Lexington, MA, U.S.A.). The iodine solutions used were: iodine 0.1 N (BDH) solution containing 0.05 M iodine in a 2% KI aqueous solution and concentrated iodine solutions (CIS). CIS is a concentrated iodine solution which contains 20% w/v iodine and 35% w/v KI. This solution was diluted with water to obtain CIS 1:1, CIS 1:2, and CIS 1:3.

Preparation of iodine matrices was carried out according to the following methods.

(a) By iodine incorporation during polyurethane polymerization: Hypol prepolymer (9.2 g) was mixed using an electrical mixer (Heidolph digital mixer with pedal) in a beaker for about 30 s. 6 g of either distilled water, for blank preparation, or iodine solution, for iodine matrix preparation, was added with vigorous mixing, and the mixture was poured between two specially designed plates, in order to obtain matrices of required thickness.

(b) By immersion of the preformed polymer in iodine solutions: Polyurethane matrices prepared with water (blank) were dipped during a controlled period of time (1 h) in iodine solutions containing various concentrations of KI and iodine (iodine BDH or CIS solutions). The matrices were left to dry at controlled room temperature and humidity for 48 h.

IR spectroscopy: IR spectra of thin iodine matrices prepared by incorporation or immersion were recorded in an IR apparatus (Perkin Elmer) and were compared to those of matrices of polyurethane without iodine.

TABLE 1

Inhibition zone diameter (mm) of S. aureus growth produced by Iodine polyurethane delivery systems of 7 mm diameter

Preparation method	Iodine conc. [a] (mg/g)	Inhibition zone (mm)
Incorporation	19	12
	24	18
	35	22
	70	27
Immersion	6	12
	21	19
	32	28
	43	35
	64	54

[a] Iodine concentration determined by titration with sodium thiosulphate.

Antimicrobial test: The antimicrobial assay was conducted according to the European Pharmacopoeia, Biological Tests (11th European Pharmacopoeia, 1971). *Staphylococcus aureus* bacteria were incubated at 37°C for 8–10 h in 0.8% nutrient broth to yield a culture of $> 10^8/cm^3$. The bacterial culture was mixed 1:10 with 1% agar/0.8% nutrient broth at 45°C. This solution was poured into petri dishes, and a patch was placed in the middle of the agar surface. All of the patches were of 1 mm thickness and 0.7 cm

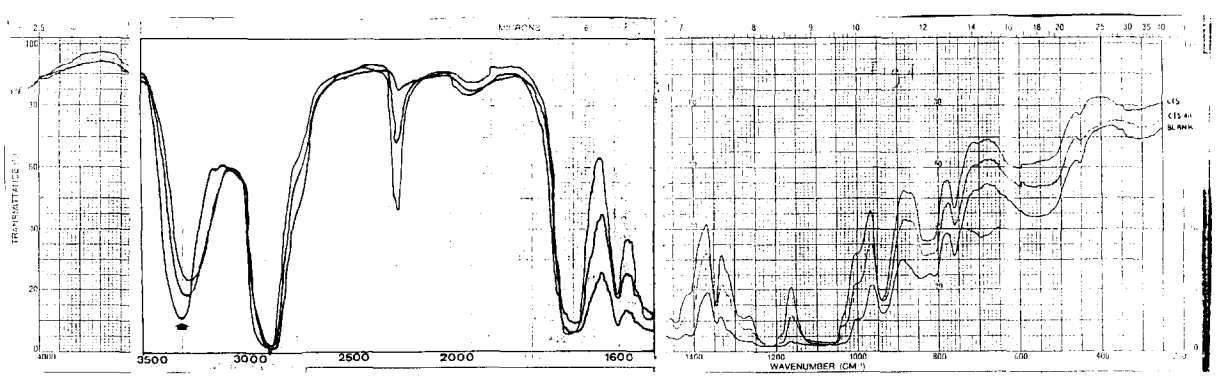

Fig. 1. The shift of the N-H IR band in the iodine-polyurethane matrices prepared by incorporation, as compared to a polyurethane matrix (blank).

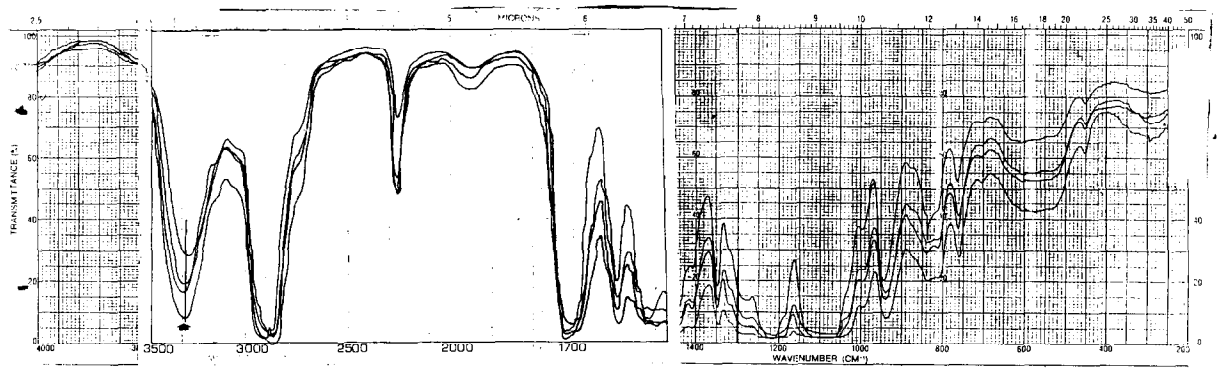

Fig. 2. IR spectra of iodine matrices prepared by incorporation of iodine solutions of various concentrations.

diameter. The dishes were incubated at 37°C for 48 h and the diameter of the inhibition zone was measured. Five petri dishes were used for each measurement.

Antimicrobial activity: The results of the antimicrobial activity are given in Table 1. The systems tested were of the same thickness (1 mm) and diameter (0.7 cm). It was not possible to obtain identical concentrations of iodine for the two methods of preparation; a comparison was made for similar concentrations. It can be seen from the results in Table 1 that antimicrobial activity was greater in patches prepared by immersion.

IR spectra of iodine polyurethane matrices: Fig. 1 shows the IR spectra of three matrices prepared by iodine incorporation during polyurethane polymerization: the blank matrix and iodine matrices I and II. The IR spectrum of the polymer (blank) used for incorporation of iodine is characterized by a large number of vibrational absorption bands with frequencies in the range of 3400–800 cm^{-1}. These bands are correlated to the stretching and bending of the interatomic covalent bonds. Such bonds are the N-H at 3300 cm^{-1}, C-H at 3000 cm^{-1} and C = O at 1700 cm^{-1}. Examination of the IR spectrum revealed that treatment of the polymer with concentrated solution of iodine produced some structural changes in the polymer. It appears that iodine produced a shift of the N-H stretching band to a lower frequency.

From Fig. 1, it can be seen that as the concentration of iodine increases, there is a rightward shift of the peak to a higher wavelength. This is further illustrated in Fig. 2, which shows the IR spectra of iodine matrices prepared by incorporation of the CIS solutions. There are known situa-

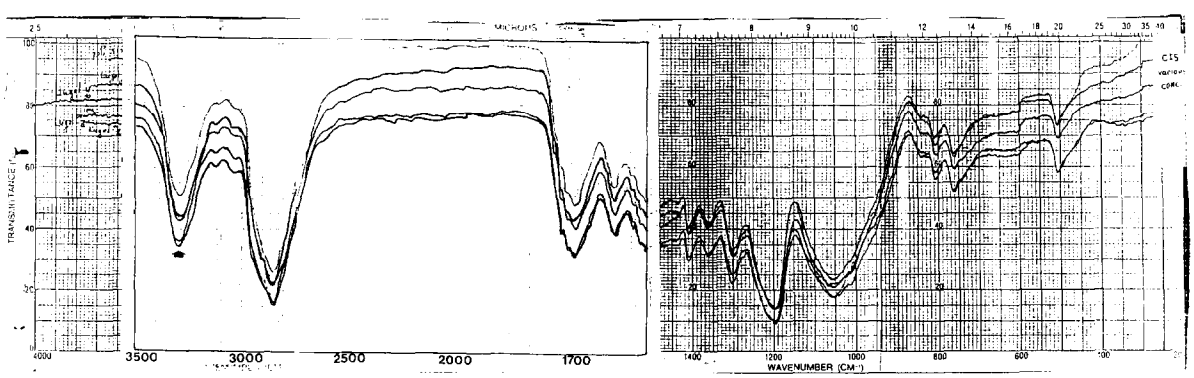

Fig. 3. IR spectra of iodine matrices prepared by immersion of the prepared matrix in iodine solutions of various concentrations.

tions in which the location of a certain absorption bond, such as N-H or C = O, is altered by the effect of hydrogen bonding, or by the environment with the structure (Burger et al., 1973; Schenck et al., 1979). The formation of a complex within an intramolecular hydrogen bond, which takes place between the lone pair electrons of iodine and amine hydrogen, is suggested as an explanaton for the behavior of systems prepared by incorporation of iodine during polymerization.

Fig. 3 presents the spectra of matrices prepared by immersion. Here it can be seen that the same absorption spectra were obtained for all three patches, and that the presence of iodine does not effect the IR absorption of the blank polymer. This behavior indicates that iodine is not bound to the polyurethane polymer.

These results can explain the difference in antimicrobial activity of the two patch types. When the incorporation method was used for preparing the patches, the iodine was strongly bound to the polymer. In contrast, iodine in patches formed by the immersion method was all available to act as an antiseptic.

In conclusion, for the same concentration of iodine in the polyurethane matrix, a different antimicrobial activity is obtained by using different methods of preparation. This must be kept in mind when polyurethane-iodine patches are chosen for antiseptic purposes.

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