NOTES

Delivery Behavior of Isoflavone Loaded Beads with Ethylcellulose/ Poly(ethylene glycol)

INTRODUCTION

Recently, attention has been focused on employing cheap raw materials and simplifying the formulations for controlled release therapies. Ethylcellulose (EC) has been widely used for matrix of drug delivery system (DDS).[1,2]

Isoflavones (Fig. 1) extracted from the roots of pueraia have been used to treat cardiacs.[3] Drug loaded beads have aroused interest as potent drug matrixes that have a desirable release profile. In the present study, isoflavone loaded beads were prepared by employing ethylcellulose/ poly(ethylene glycol) (EC/PEG) as the matrix, while the *in vitro* release behavior was investigated.

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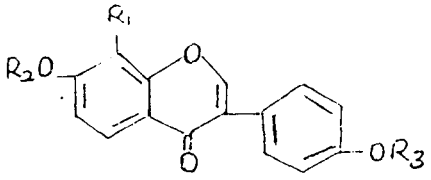
EXPERIMENTAL

Materials

Isoflavones were extracted from pieces of the roots of pueraia (Hong Qiao Chinese Medicine Manufacturer, Shanghai). EC (9–10 and 40–100 cp viscosity), of 5% toluene/ethanol (80/20 w/w) solution at 25°C and PEG with average molecular weight of 4000 were used as matrixes. Other reagents applied were chemical grade.

Preparation of Isoflavone Loaded EC/PEG Beads

EC and PEG 4000 were dissolved in ethanol and then isoflavones were added with agitation at 30–40°C. After the drug dissolved completely, ethanol was evaporated under stirring to obtain drug loaded beads.



Analogue	R_1	R_2	R_3
Daidzain	H	H	H
Daidzin	H	glucose	H
Pucrarin	glucose	H	H
Diadzein 4', 7 diglucoside	H	glucose	glucose

Figure 1 Main components of isoflavones.[5]

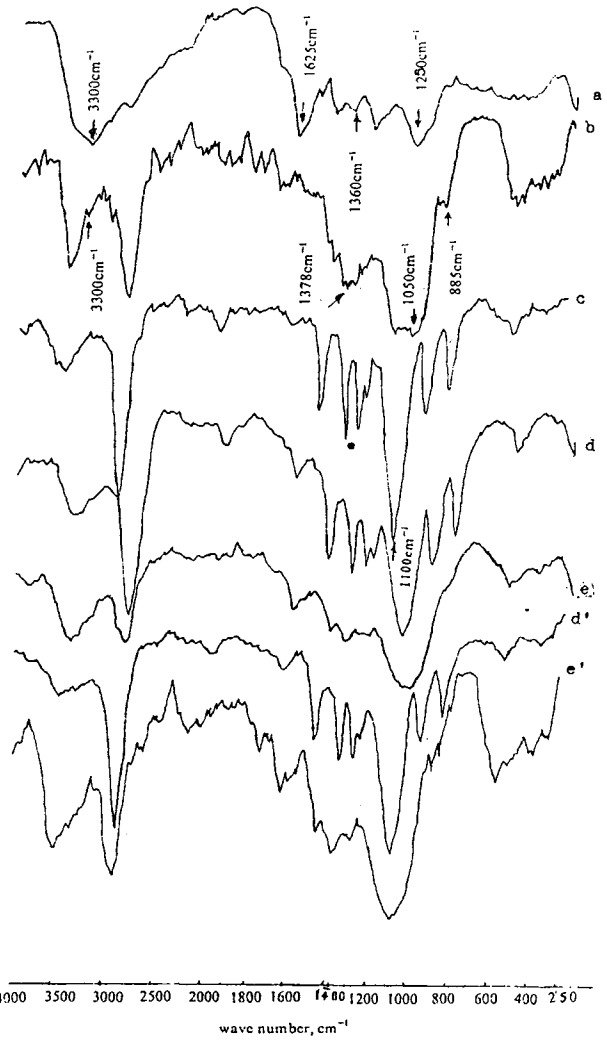


Figure 2 IR spectra of isoflavones from (a) *Radix pueraia* extract, (b) EC, (c) PEG, (d) drug loaded beads with PEG, and (e) that with EC/PEG in comparison with mixtures of drug with (d') PEG and (e') EC/PEG, respectively.

Release Study

The release experiments were performed in a rotating shaker (100 rpm) containing artificial gastric liquid (pH 1.2) at 37 ± 0.5°C. The drug loaded beads were added into the shaker. A 4-mL aliquot of medium was withdrawn at different time intervals and isoflavone content assayed spectrophotometrically at 250 nm.

IR Spectra

The IR spectra of EC, PEG, and drug loaded beads were determined by using a Hitachi 270-50 infrared spectrophotometer.[4]

X-Ray Diffraction

The X-ray diffraction of EC, PEG, and drug loaded beads were carried out with a Raghu 2308 Diffractometer.

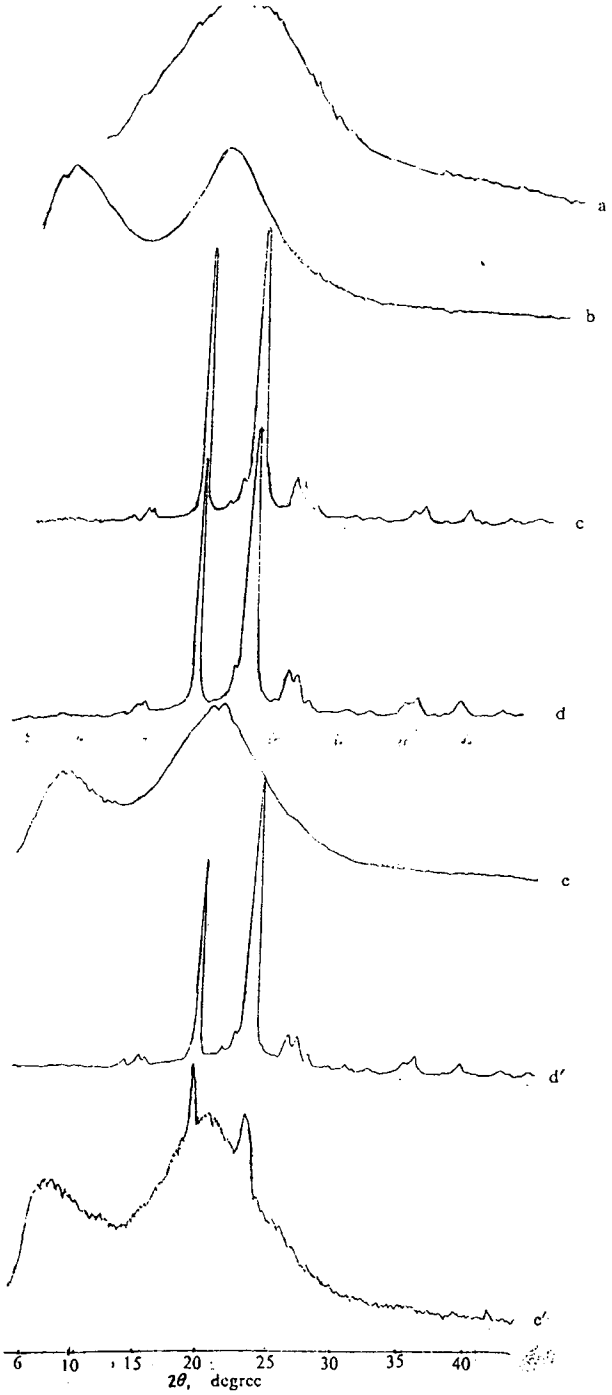


Figure 3 X-ray diffraction spectra of isoflavones from (a) *Radix pueraia* extract, (b) EC, (c) PEG, (d) drug loaded beads with PEG, and (e) that with EC/PEG in comparison with mixtures of drug with (d') PEG and (e') EC/PEG, respectively.

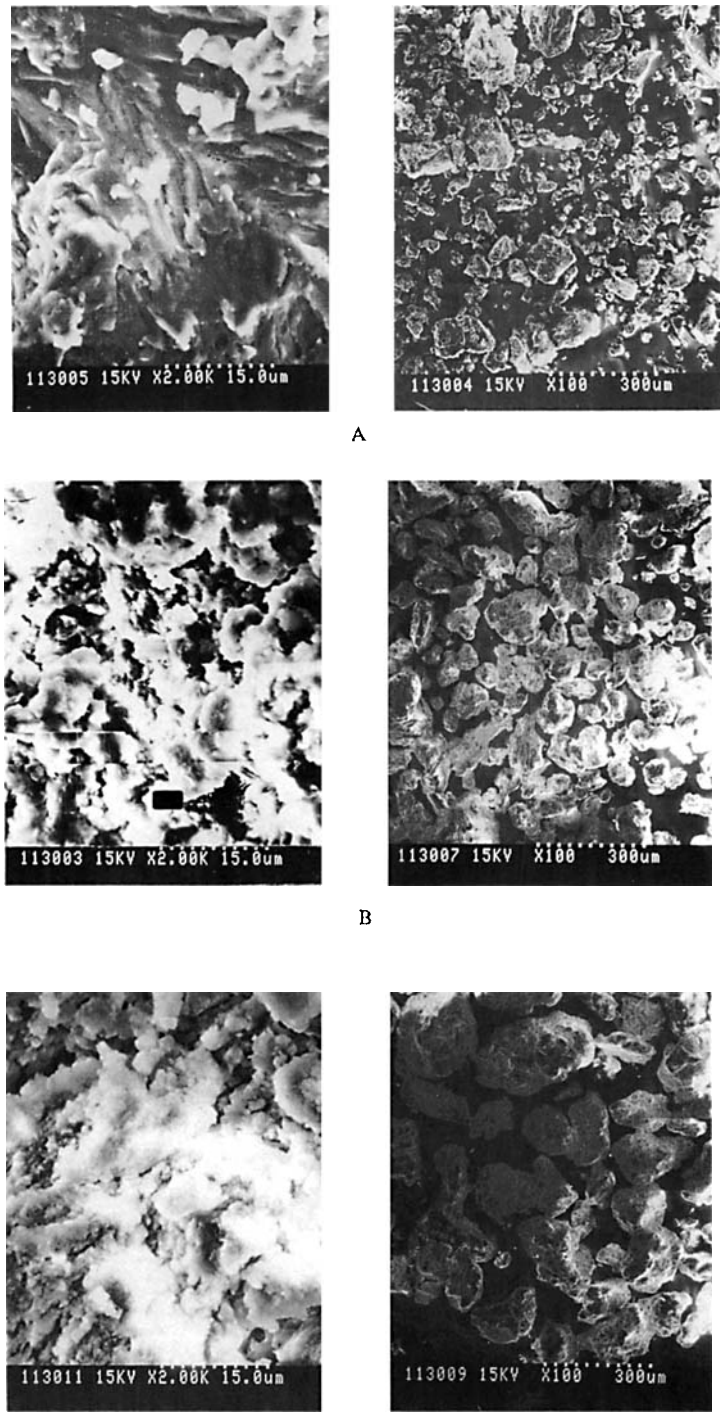


Figure 4 SEM micrographs of isoflavones from *Radix pueraia* extract loaded beads with (A) PEG, and with (B) EC/PEG (original; B released for 1 h), (C) at drug, PEG = 1 : 10 and drug : EC : PEG = 1 : 5 : 0.4 by weight, respectively.

Scanning Electron Microscopy (SEM) Observation

The surface morphology of beads was examined using a scanning electron microscope (Hitachi Model 1650). Samples were mounted on metal stubs, vacuum coated with gold film, and then observed.

RESULTS AND DISCUSSION

Characteristics of Drug Loaded Beads

Figure 2 shows the IR spectra of (a) pueraia extract, (b) EC, (c) PEG, (d) drug loaded beads with PEG, and (e) that with EC/PEG in comparison with mixtures of drug with (d') PEG and (e') EC/PEG. There are characteristic peaks at 3300 cm^{-1} (OH stretching), 1625 cm^{-1} (C=C stretching vibration in pyrone), and 1360 and 1200 cm^{-1} (C—O, OH stretching in phenol) in the spectrum of the pueraia extract [Fig. 2(a)]. The spectrum of EC [Fig 2(b)] is characterized by the existence of peaks at 3300 cm^{-1} (OH stretching), 1378 cm^{-1} (—CH), 1050 cm^{-1} (C—O—C in cellulose derivatives), 1000–1100 cm^{-1} (pyran linking), and 885 cm^{-1} ($-OC_2H_5$). In PEG [Fig. 2(c)] the most intense band is the aliphatic C—O—C stretching vibration at 1100 cm^{-1}; the O—H stretching vibration is found as broad between 3300 and 3600 cm^{-1}. In comparing the drug loaded PEG beads [Fig. 2(d)] with the drug mixture with PEG [Fig. 2(d')], their characteristic bands are alike. However there is variation in the range of 1500–2500 cm^{-1} from spectra of the drug loaded beads with EC/PEG [Fig. 2(e)] to the mixture of drug and EC/PEG [Fig. 2(e')].

Figure 3 shows x-ray diffraction patterns of the corresponding sample (Fig. 2). Results indicate that diffraction of the drug loaded beads with EC/PEG [Fig. 3(e)] is different from that of the corresponding mixture [Fig. 3(e')] in lack of separable peaks at $2\theta = 18°$ and 23° of PEG. That contrasts to the similar diffraction spectra of the drug loaded beads with PEG and the mixture of drug and PEG. There may be some kind of interaction between the drug and PEG with EC. The result coincides with the variation in IR spectra of the drug loaded beads with EC/PEG added to the mixture.

Surface Morphology of Drug Loaded Beads

SEM micrographs of surface morphology are shown in Figure 4. The drug loaded beads with EC/PEG were more even in size in comparison with that with PEG matrix. This may be attributed to the specific interaction among the drug and PEG with EC.

Release Behavior of Isoflavones from Beads

Figure 5 show the release behavior of isoflavones from the drug loaded beads. Here an initial burst release followed

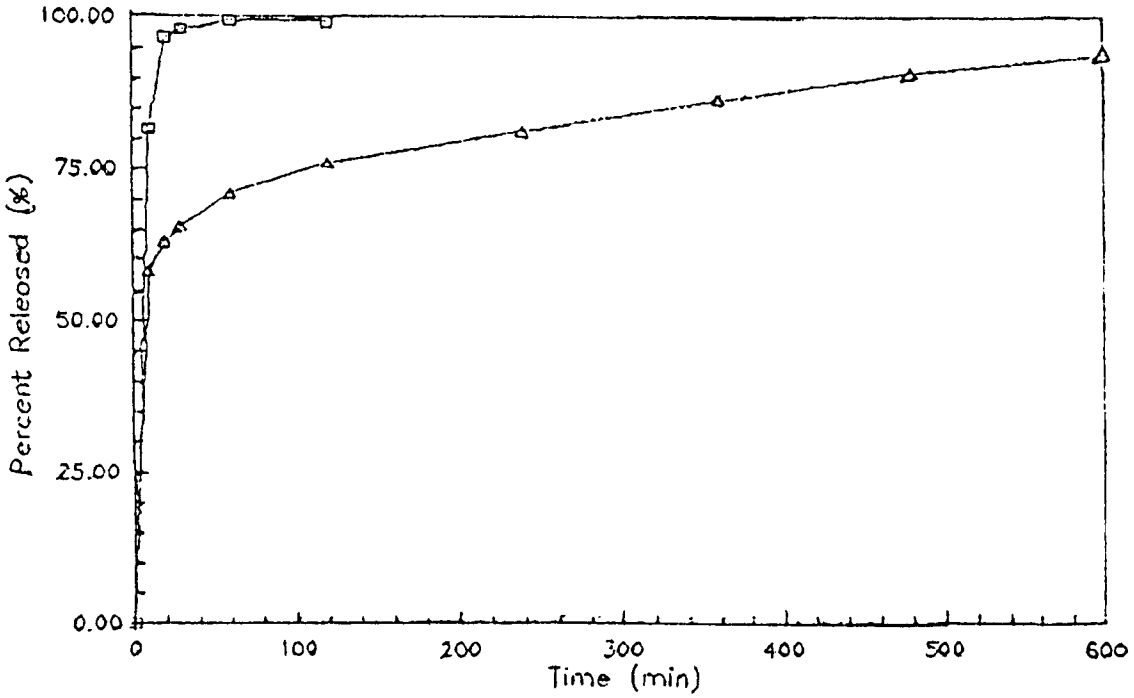


Figure 5 Release of isoflavones from pueraia loaded beads with (□) PEG (drug : PEG = 1 : 10 w/w) and beads with (△) EC/PEG (drug : EC : PEG = 1 : 5 : 0.4 w/w), respectively, as a function of time.

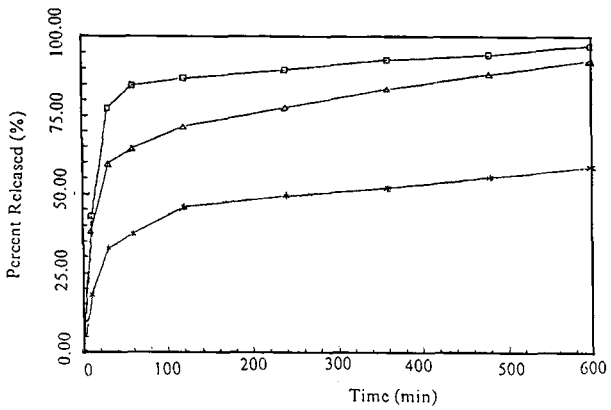


Figure 6 Release behavior of isoflavones from pueraia loaded beads of EC/PEG matrix with different PEG amounts: drug : EC : PEG = (□) 1 : 5 : 1; (△) 1 : 5 : 0.4; (*)1 : 5 : 0.1.

by a slow release of isoflavones is evident in the artificial gastric liquid (pH 1.2) at 37 ± 0.5°C. All of the drug was exhausted from the beads within 1–10 h. Data reveal that PEG has a promoting function for drug delivery, because of its solubilizing effect to the drug. Therefore the percent release of isoflavones can be controlled by the composition of the EC/PEG matrix (cf. Fig. 6).

The results demonstrate that *in vitro* a near zero-order release of isoflavones is observed with PEG and EC/PEG beads. However the release of the drug from PEG beads was rapid. Thus it appears that the mechanism of drug release may be due to disintegration of PEG matrix or diffusion through the swollen EC/PEG matrix in the pH 1.2 medium. The latter case can be demonstrated in Figure 4(c).

CONCLUSIONS

Isoflavones can be dispersed in EC PEG matrix to prepare drug loaded beads. A potent pattern of isoflavones released will be obtained from the optimal formulation. The drug delivery system of pueraia extract may be a promising candidate from Chinese traditional and herbal drug practices applied to modern oral drug release.

References

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