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KINETICS OF DRUG RELEASE FROM ISONICOTINIC ACID HYDRAZIDE MICROCAPSULES

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ABSTRACT

Isonicotinic acid hydrazide is encapsulated by emulsification - solvent evaporation technique using Eudragit RS 100 as coating polymer.An empirical relationship between drug loading and drug diffusibility through the polymer matrix was developed.

INTRODUCTION

There are some reports by Benita et al.(1),Fouli et al.(2),Pal et al.(3) relating to Eudragit microcapsules.However,most of these microcapsules had been prepared by coacervation method.We have already reported the microencapsulation of drugs using Eudragit RS by emulsification-solvent evaporation technique (4) in the oil phase.As the drug loading plays an important role in the control of drug release rate, the main objective of the present investigation is to establish an empirical relationship between drug loading and drug diffusibility through the polymeric matrix.

EXPERIMENTAL

Preparation of Microcapsules

Microcapsules were prepared by the same manner as reported previously by Pal et al. (4).

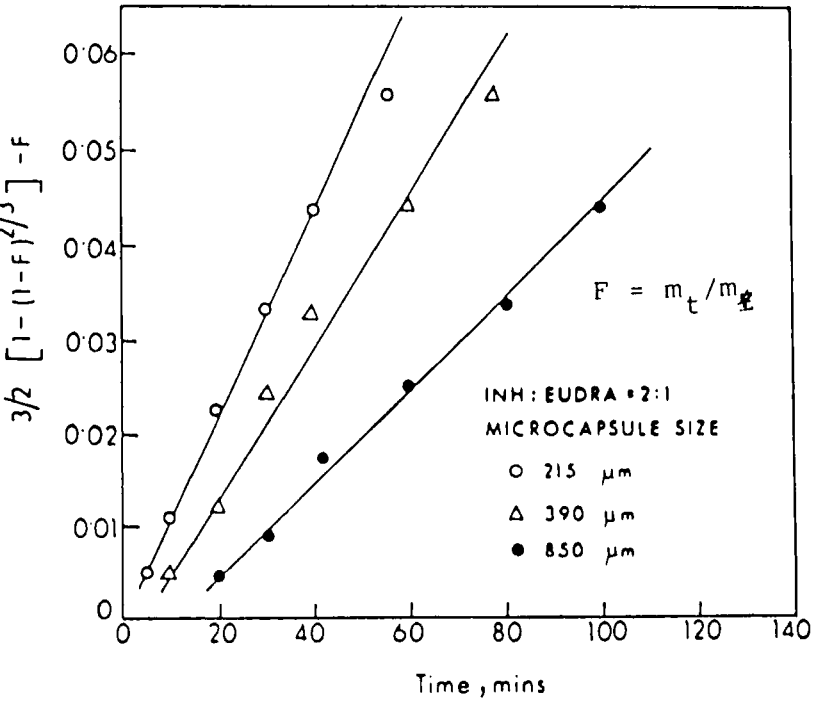

FIGURE 1

Analysis of Drug Release Profile According to Baker Lonsdale Model when Drug Polymer Ratio is 2:1

Dissolution Study

The dissolution of Isoniazid from the microcapsules was studied at pH 7.2 with the modified flask method. (5).

RESULTS AND DISCUSSION

The diffusional coefficient (D_i) was evaluated using the Baker-Lonsdale model for spherical matrix release kinetics (6,7), as given below

$$1.5 \left[1 - (1 - m_t / m_\infty)^{2/3} \right] - m_t / m_\infty = 3D_i C_s t / r_o^2 A \quad ---(1)$$

for $o \leq m_t / m_\infty \leq 0.5o$, and where m_t and m_x are the amounts of drug release at time t and at infinity time (∞)

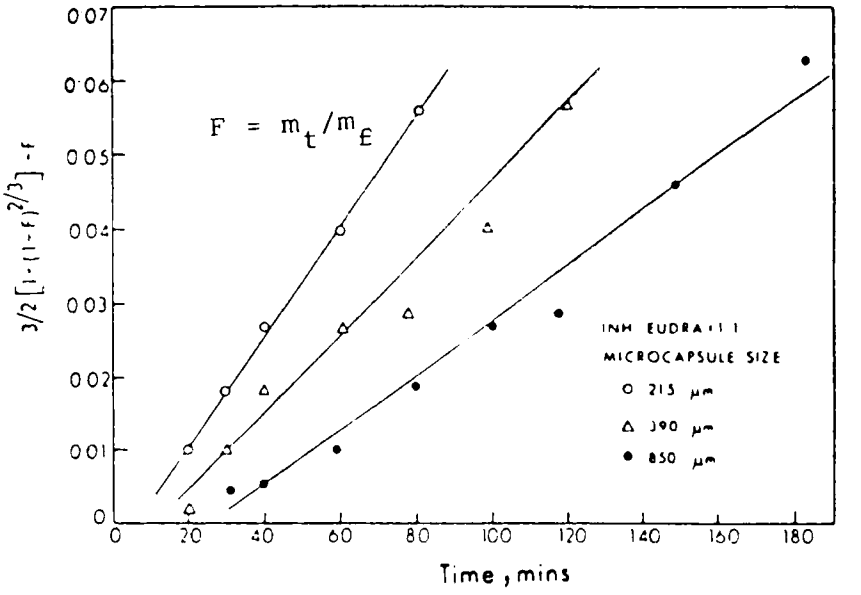

FIGURE 2

Analysis of Drug Release Profile According to Baker Lonsdale Model when Drug Polymer Ratio is 1:1

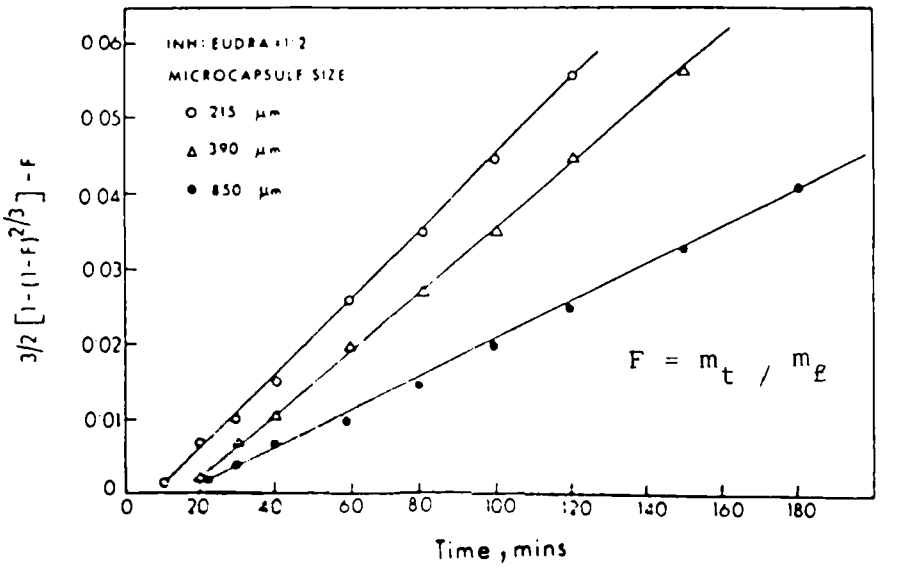

FIGURE 3

Analysis of Drug Release Profile According to Baker Lonsdale Model when Drug Polymer Ratio is 1:2

TABLE 1

PHARMACOKINETIC DATA OF ISONIAZID MICROCAPSULES

Drug : Polymer	Microcapsules (μm)	K_{BL} (min^{-1})	Log K_{BL}	A (gms/c.c)	Log A	Density (gms/c.c)
2 : 1	215	1.183489×10^{-3} (0.9955)*	-2.9268	0.7458	-0.1273	1.3926
	390	7.1784003×10^{-4} (0.991)*	-3.1439	0.6955	-0.1577	1.1130
	850	5.405240×10^{-4} (0.9953)*	-3.2671	0.6570	-0.1824	1.0015
1 : 1	215	7.405323×10^{-4} (0.954)*	-3.1304	0.5368	-0.27018	1.4565
	390	4.640779×10^{-4} (0.9795)*	-3.3334	0.4921	-0.3079	1.1265
	850	3.139626×10^{-4} (0.9887)*	-3.5031	0.4735	-0.3246	1.0020
1 : 2	215	4.763424×10^{-4} (0.9984)*	-3.3220	0.4240	-0.3726	1.5223
	390	3.934423×10^{-4} (0.9953)*	-3.4051	0.3888	-0.4102	1.2360
	850	2.470300×10^{-4} (0.9941)	-3.6072	0.3740	-0.4271	1.1526

* Correlation Coefficients for $0 \leq \frac{m_t}{m_\infty} \leq 0.50$

respectively. C_s is the drug solubility in the dissolution medium, r_o is the radius of the matrix, A is the drug loading or initial drug content per unit volume of the matrix and the Baker-Lonsdale rate constant, $K_{BL} = 3 C_s D_i / r_o^2 A$ ---- (2)

The drug release data were plotted according to Equn. (1) and are shown in Fig. Nos. 1 to 3. Fig. Nos 1 to 3 show that drug loading affects the release rate in such way that the term D/A in Equn.(1) increases as A increases, suggesting that drug diffusivity may be increased exponentially with increasing drug loading in the microcapsule system. The values of K_{BL} (Table 1.) determined as the slope of the plot of Equn. (1). An empirical relationship between D and A has been established . $D = k A^n$ where k is a constant , and $K_{BL} = 3 C_s k A^{n-1} / r_o^2$ ---- (3) , where n could be determined from the log-log plot of K_{BL} and A.

For the microcapsule size of 850 μm the value of n was found to be 2.6597 for the present investigation. These observations agree with the results reported by Luzzi et al. (6) and Tsai et al. (7).

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