Results and discussion

The release pattern of formulation in different drug-polymer matrix in simulated intestinal fluid (SIF) and simulated gastric fluid (SGF) showed in Figure 1 and 2. We found that the polymer matrix can sustain the drug release in longer than 12 hours at pH 1.2. The polymer matrix is intact. It started by the penetration of water into tablet. The drug dissolved and diffused from the intact matrix. In SIF, the ratio 1:2 is the best formulation for 12 hours complete release but the ratio 1:3 releasing time is longer than 12 hours. The percent release correlated with time by constant rate. From an observation, the matrix eroded outer part of the barrier and at the same time the water penetrated the matrix and formed gel. The gel eroded while releasing drug. Gel forming will block the drug with no diffusion and control the rate of water permeate. When the gel eroded and dissolved, water permeated into inner core to form newer gel to control the release till it dissolved completely.

The viscosity measurement from the dissolution medium was very low. (1-3 cps) It behaved newtonian flow. Because of the gel dissolved very small amount and generated very low viscous liquid. On the contrary that the matrix is insoluble or nearly insoluble at the very low pH (less than 2). The gel layer was very thick so the drug can not dissolve well. But the pH 4.5, 6.5 and 7.5, the gel forming generated and dissolved on the same time. The mechanism of release will be discussed.

From different mechanism of release at the different pH , it can prove from data that the matrix was intact at pH 1.2 from observation and splitting at the middle part. The phenomena was the splitting of tablet in two parts or called burst effect. Herman and Remon (1989) described by the reason that applying very low force or the very large particle of matrix. But in this experiment the splitting part were intact like a denatured rubber. It supposed to be the insoluble properties of alginate in pH less than 2. At pH 4.5, 6.5 a remarkable increasing release rate was shown in figure 3 and 4 because of the forming gel is lesser at the higher pH . At pH 1.2 when applying the Higuchi equation with square root time we did not obtain straight line (Figure 5) that correspondent to $Q = kt^{1/2}$. (equation 1) It could not explain by the release from inert and intact matrix. It might be the combined effect from the diffusion through hydrogel barrier. But pH between 1.2 and 7.5 the mechanism of release followed the equation below. (Peppas, 1989 and Colombo et al 1992)

$$Q = k_1 t + k_2 t^{1/2} \quad \text{equation 2}$$

Q = amount drug dissolved

k_2 = Diffusion constant through insoluble matrix

k_1 = Erosion constant due to gel eroding

Dissolution data at diffferent times from different pH can give different value of k_1 and k_2. Table 1 shows these two values at different pH. These values are calculated by computer programme to fit data with equation 2 and explain that at which pH which mechanism of release is superior than the other one. At the low pH (1.2) the diffusion constant is very high. It does not show the erosion in some case but in some cases (drug/polymer 1:2 and 1:3) the erosion constant appeared. At the higher pH the erosion constant is leading and some pH showed some small diffusion constant.

In intestinal fluid, the gel formation is forming and swelling outer part of tablet. After that it dissolved by mechanical rotation of paddle and circulation of water to be sink condition. We found that the time release pattern changed from curvature to be more striaght line especially nearly the end of 10 to 12 hours. The relation will be $Q = kt$. From this equation the release of drug from matrix by the mechanism of erosion mostly. The sequence of mechanism started with the solvent penetration into tablet. Then matrix forms gel. Gel dissolved together with drugs. Gel was a barrier to control the rate of diffusion outside of drug and the rate of water permeate into tablet. When the gel was eroded the solvent permeate more into core of tablet. The new layer of gel forming will control the rate of release until the complete dissolved tablet.

From this experiment we can conclude that the hydrophilic polymer matrix can described the mechanism of release in two terms named erosion constant and diffusion constant. These two values are related to each one when one shows very high value the other one shows low value at different pH (Table 1).

Table 1 : Erosion and diffusion constant obtained from $Q = k_1 t + K_2 t^{1/2}$ by computer aids. (nonlinear regression, constrainst > 0)

Drug/polymer		Erosion constant	Diffusion constant
1: 1	pH 1.2	0	21.7829
	pH 4.5	10.3923	0
	pH 6.5	16.2683	0
	pH 7.5	9.943 0	0
1:2	pH 1.2	1.1757	17.8697
	pH 4.5	8.1033	3.0849
	pH 6.5	10.5173	0
	pH 7.5	9.6554	0
1:3	pH 1.2	1.3272	1.3272
	pH 4.5	6.1974	0
	pH 6.5	9.4258	0
	pH 7.5	7.4407	0