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THE EFFECT OF NONIONIC WATER SOLUBLE CELLULOSE POLYMERS ON THE SETTLING OF DRUG PARTICLES

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ABSTRACT

The influence of nonionic water soluble cellulose polymers, hydroxypropylmethylcellulose and hydroxyethylcellulose, on the settling of ibuprofen particles and the sediment behavior has been investigated. Results for hydroxypropylmethylcellulose systems showed that the higher the viscosity of the medium the slower the particle settling velocity. Heavily caked suspensions were obtained after particles settling. It was probably due to the gel network formation in the sediment.

INTRODUCTION

Nonionic water soluble cellulose polymers are the common use suspending agents in controlling particles settling[1-6]. It has been demonstrated previously that these polymers are adsorbed at the particle interface

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and affect the particle stability by steric stabilization or flocculation depending on the concentration used[7,8]. The present work investigates the suspending effect of two groups of nonionic water soluble cellulose polymers on the settling of ibuprofen particles and the sediment behavior.

MATERIALS AND METHODS

The nonionic water soluble cellulose polymers used were hydroxypropylmethylcellulose (HPMC, Pharmacoat 603, 606 and 615) and hydroxyethylcellulose (HEC, Natrosol 250R L and J) as described previously[7,8]. The drug used was ibuprofen[7,8].

Suspensions of ibuprofen were prepared according to the previous procedures[7,8]. The concentration range studied for HEC was from 0.1 to 3.0 g/dl and for HPMC was from 0.5 to 3.5 g/dl. Sedimentation volume (SV) and redispersibility (RV) were recorded as described previously[7,8].

RESULTS AND DISCUSSION

The settling curves plotted as SV against time are shown in Figures 1, 2 and 3 for HPMC 603, 606 and 615 systems respectively. The curves show that the higher the viscosity of the medium the slower the particle settling velocity which is as predcited by Stocks' law.

In the settling of the ibuprofen particles in the HEC solutions studied, it was difficult to justify the

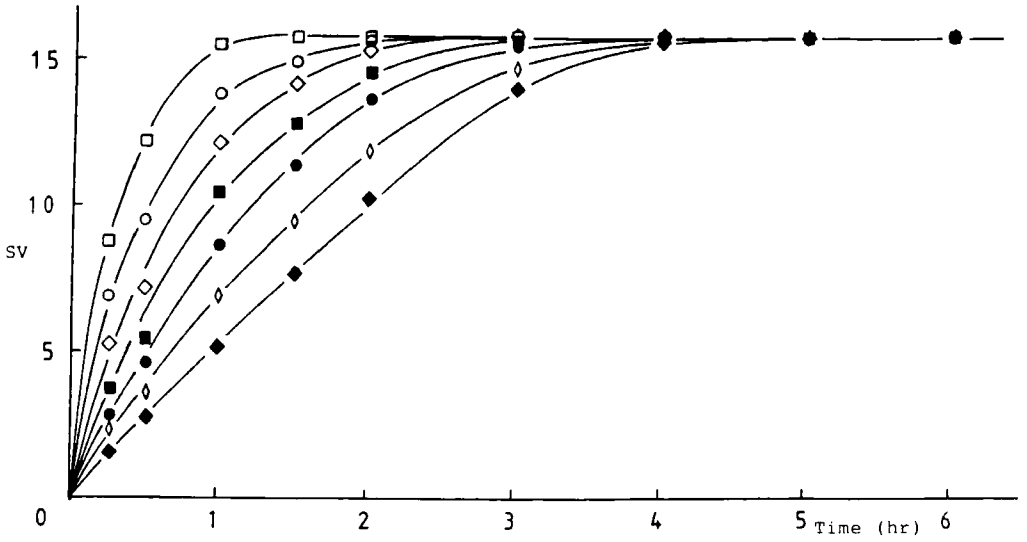

Fig. 1 Settling curves for ibuprofen in the presence of HPMC 603.

	□	○	◇	■	●	◊	◆
Concentration (g/dl):	0.5	1.0	1.5	2.0	2.5	3.0	3.5
Viscosity (10^{-3}Nm^{-2}s):	0.6	1.3	1.9	2.5	3.5	4.2	5.4

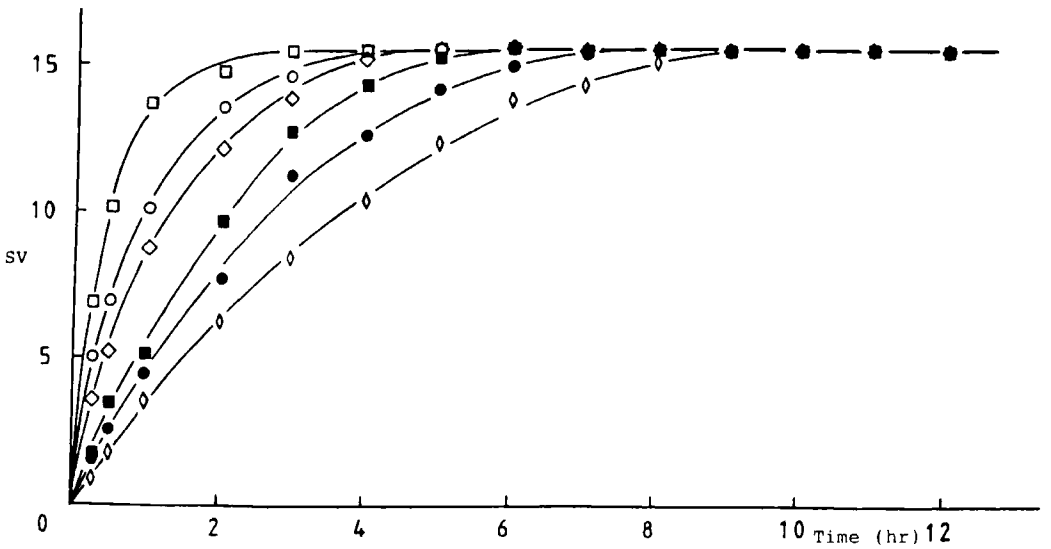

Fig. 2 Settling curves for ibuprofen in the presence of HPMC 606.

	□	○	◇	■	●	◊
Concentration (g/dl):	0.5	1.0	1.5	2.5	3.0	3.5
Viscosity (10^{-3}Nm^{-2}s):	1.4	2.1	3.5	7.5	10.3	14.4

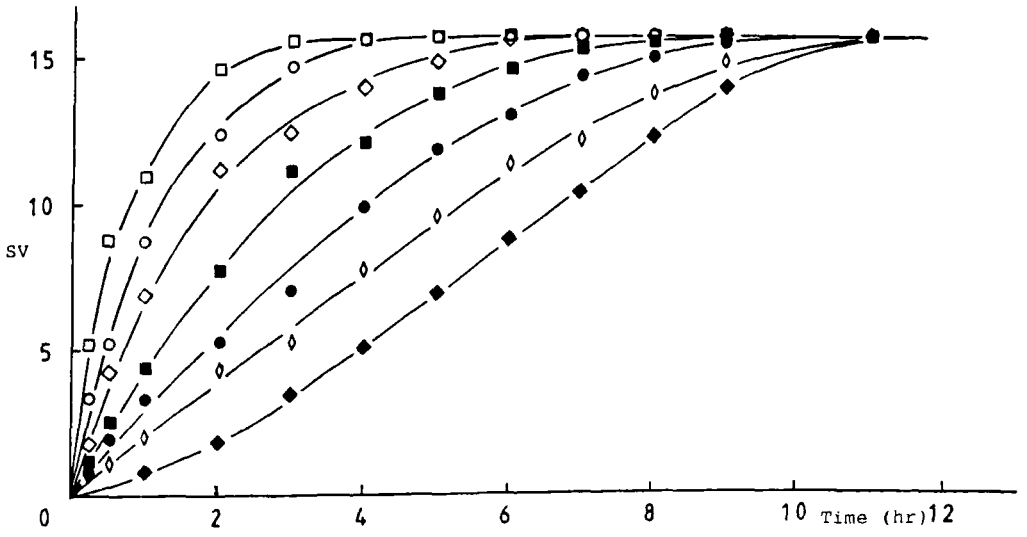

Fig. 3 Settling curves for ibuprofen in the presence of HPMC 615.

	□	○	◇	■	●	◊	◆
Concentration (g/dl):	0.5	1.0	1.5	2.0	2.5	3.0	3.5
Viscosity ($10^{-3}Nm^{-2}s$):	2.5	3.7	7.0	12.5	19.5	32.0	51.1

measurements due to most of the aggregated particles floated on the upper part of the suspensions. However, from the sedimentation volumes, it showed a voluminous structure of aggregates in the polymer concentration range of from 0.1 to 1.5 g/dl; whereas, from 2 to 3 g/dl, in the majority cases, the particles were suspended in small structured flocs and a small portion of the particles settled down forming a hard caked sediment.

The redispersibility of the HPMC-ibuprofen suspensions after 36,000 revolutions of redispersion the sediments were resuspended little. The sediments were heavily caked. The appearance of the surpernatants after redispersion showed that a greater degree of

turbidity was found at low concentrations than at high concentrations.

It was suggested previously that multilayer adsorption will occur at high polymer concentrations[7]. Therefore, in this study, as polymer concentration increases, more polymers are adsorbed on to the surface of the particles forming a multilayer. When the particles are settled, the adsorbed polymers form a large structure of molecular network in which the interwoven polymer chains in the network hold the particles strongly. This is somewhat like the approach of gel formation of the cellulose polymers in the sediment.

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