TO STUDY THE EFFECT GELLAN GUM, HPMC AND $CaCO_3$ ON FLOATING LAG TIME, GELATION TIME AND WATER UPTAKE

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ABSTRACT

The *in-situ* hydrogel drug delivery system has attracted attention from more and more researchers in recent years. In the present research work effect of gellan gum, $CaCO_3$ and HPMC on water uptake time, gelation time as well as floating lag time of *in-situ* hydrogel preparation of nizatidine was studied. Various concentration of gellan gum, HPMC and $CaCO_3$ were used in different formulations. Data showed that both the gelation time and the floating-lag time could be minimized through increased amount of HPMC. It has been discovered that the incorporation of divalent (Ca2+) ions into gellan gels results in the gels becoming more robust. The water uptake by the gels were low, L1 showed highest water uptake of 13% (2 h) and L4 showed least water uptake of 4.6% (2 h).

Key Words: *in-situ* hydrogel, HPMC, floating-lag time, water uptake.

INTRODUCTION

Recent years have seen a rise in curiosity regarding the study of in-situ hydrogel drug delivery systems. Simple application, high local drug concentration, increased drug retention time, decreased drug dosage in vivo, strong biocompatibility, as well as enhanced patient compliance are just some of the benefits that in situ hydrogels may provide for drug delivery applications. Since the polymer components comprising the in-situ hydrogel system are themselves in a solution, suspension, or semi-solid state, they are capable of undergoing a phase shift at the site where they are administered within seconds after dosing. After the formulation is made, the medicine may be delivered to the desired areas of patients with ease because of the formulation's liquid state. [1]

Gellan Gum is a bacterial exopolysaccharide that has been around since its discovery in 1978 and may be bought in stores in the United States and Japan. Gellan gum is made commercially from the Sphingomonas elodea species by an aerobic submerged method. Gellan gum is produced in factories using bacteria called S. paucimobilis. [2,3]

Because of its water solubility, biocompatibility, transparency, and rheological qualities, hydroxypropyl methylcellulose (HMPC) finds widespread use in pharmaceutical formulations. [4]

Calcium carbonate is one of the most often utilized chemicals in biological mineralization processes. Calcite, aragonite, along with vaterite are the three anhydrous polymorphs of calcium carbonate. Calcite has the highest thermodynamic stability and is thus the most frequent. Unlike aragonite, which often forms in orthorhombic crystals, its most common crystal shapes are rhombohedral and scalenohedral. Monocrystalline particles best describe calcite and aragonite. The polycrystalline spheres formed by the crystallization of vaterite, the least thermodynamically stable polymorph, are slowly dissolved and recrystallized from aqueous solutions into the other two, more stable polymorphs. [5]

METHODOLOGY

Determination of Gelation time

In order to determine the amount of time necessary for in situ gelation, the tube inversion approach was utilized. It was necessary to alter the temperature of the water bath based on the gelation temperature, which had previously been estimated for in situ gels. Following the transfer of a 2 milliliter gel of aliquot, the tube had been positioned with in a water bath that was heated to a particular degree. In order to determine whether or not the substance had gelled, the test tube was turned upside down. A test tube was inverted and a flow or no flow criterion was used to determine how long the gelation process took.

The in situ gelation time of nizatidine was evaluated by gradually adding 10 ml of the formulation to a volume of 900 milliliters of buffer solution(pH 1.2) that was maintaining at 37 degree Celsius. The solution was not stirred during this process. Recording the amount of time that passes as the solution transforms into a gel is something that is done. [6]

Determination of Floating Time

We poured 10 millilitres of the formulation into the dissolution vessel, which held 900 millilitres of the HCl buffer at a pH of 1.2 and 37-degrees Kelvin. This was done with as little stirring as possible. It was determined by monitoring the passage of time how much time passed before the formulation floats to the top of the dissolving medium (the floating lagging time), as well as how long it lasted at that level (the floating duration). [7]

Evaluation of Water Up-take

In situ gel was generated in 40 millilitres of HCl buffer at a pH of 1.2 and it was employed. It was necessary to take the gel component out of the HCl buffer with a pH of 1.2 and then blot off any excess HCl solution from each batch. After determining the gel's initial density by weighing it before adding 10 ml of distilled water, we then decanted the water at intervals of 30 minutes and remeasured the gel's weight in order to evaluate the degree to which its density shifted. [8]

RESULT AND DISCUSSION

Gellan Gum's Effect on Gelation and Floating Lag Times

Formulation’s Code	Gelation time* (sec)	Floating lagtime* (sec)
L1	4.33±1	125±6

L2	3.00±1	107±8
L3	2.00±1	95±6
L4	1.33±1	82±2

*Mean±Standard deviation,n=3

The data showed a clear pattern or trend that could be seen. The floating lag time for L4 was the shortest, while the time for L1 was the longest. The formulation's viscosity was raised because of the existence of gellan gum, which was discovered by the highest amount in L4. As a direct consequence of this, the sol required a shorter amount of time to break through the surface of the medium after it had formed a cohesive gel mass. The floating lag time of the systems that were created decreased as the concentration of the polymers grew, but the conc. of the polymers had no discernable effect on the floating time.

Based on what has been said thus far, it appears that the floating lag time responds noticeably to changes in gellan gum concentration. The floating lag time of a formula is reduced when it has a larger concentration of gellan gum, and the opposite is true.

The Effect of Hydroxy Propyl Methyl Cellulose(HPMC) on The Gelation and Floating Delay Times

Formulation Code	Gelation time* (sec)	Floating lagtime* (sec)
L5	3.00±1	112±5
L6	2.00±1	105±5
L7	2.00±1	98±4
L8	2.00±1	91±6

Mean±Standard deviation,n=3

Data showed that both the gelation time and the floating-lag time could be minimized through increased amount of HPMC. The formation of a hard gel in the system is directly attributable to the existence of Hydroxypropyl methylcellulose, which may greatly, contributes to gel's viscosity. Created gel is beneficial to flotation and helps cut down on the amount of time needed to float. The concentration of HPMC was raised from 0.2% to 0.8%, which resulted in significant progress being made toward the goal of reducing the floating lag time from 112 seconds to 91 seconds. If you keep the concentration of $CaCO_3$ the same but add more HPMC, it's possible that you won't be able to lessen the floating-lag time; along with it's also possible that the formulation will sink because it won't have as much buoyancy.

Calcium Carbonate's Impact on Floating Lag Time and Gelation Time

Formulation Code	Gelation time* (sec)	Floating lag time* (sec)
L9	5.33±1	142±5

L10	4.33±1	126±7
L11	3.00±1	115±5
L12	2.00±1	104±4

*Mean±Standard deviation,n=3

The formulation contains an insoluble dispersion of calcium carbonate, which, when exposed to an acidic medium, will dissolve. This will result in the release of Ca^{++} ions that will give rise to the gelation of the polymer's known as gellan gum. It has been discovered that the incorporation of divalent ($Ca^{2+)}$ ions into gellan gels results in the gels becoming more robust.

As the quantity of calcium carbonate was raised, there was a corresponding reduction in the amount of time that passed before the water once again began to float. The decrease in floating lag time may be traced back to two factors an increase in the Ca^{2+} ion content as well as the CO_2 level. The L9 formulation has a greater gelation lag time as well as a longer floating lag time when compared to the L12 version. Therefore, it should come as no surprise that calcium carbonate has a considerable impact on the gelation and floating lag times

Measurement of water uptake

Formulation Code	% Water Uptake
L1	13.0
L2	7.9
L3	6.7
L4	4.6
L5	10.7
L6	8.7
L7	7.4
L8	5.2
L9	11.2
L10	9.1
L11	8.8
L12	8.7

After two hours, the tests revealed that L1 had taken 13% more water than L4, while L4 had only absorbed 4.6% less water than L1. When the body takes in more water, there is an increase in the amount of medication that is eliminated through the urinary tract. As a consequence of this, it is desirable for a system of sustained release to have a low water absorption because this results in a prolonged drug release.

Conclusion

In the present study the effect gellan gum, HPMC and $CaCO_3$ on floating lag time, gelation time and water uptake. It was concluded that formulation L4 demonstrated the quickest gelation time (1.33 seconds) for nizatidine in-situ gels when put in a pH 1.2 solution, whereas formulation L9 showed the slowest gelation time (5.33 seconds). The concentration of HPMC was raised from

0.2% to 0.8%, which resulted in significant progress being made toward the goal of reducing the floating lag time from 112 seconds to 91 seconds. It has been discovered that the incorporation of divalent (Ca2+) ions into gellan gels results in the gels becoming more robust. The water uptake by the gels were low, L1 showed highest water uptake of 13% (2 h) and L4 showed least water uptake of 4.6% (2 h).

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