PROCEEDING

THE 2ND INTERNATIONAL CONFERENCE ON

PHARMACY AND ADVANCED PHARMACEUTICAL SCIENCES

Book 1:
Pharmaceutical Science

Faculty of Pharmacy
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STRILIZATION HEAT EFFECT TO GEL BASE PHYSICAL PROPERTIES: ELLING AGENT CMC NA AND CA ALGINATE CASE STUDY

Sri Hartati Yuliani, Achmad Fudholi, Suwijiyo Pramono and Marchaban
Faculty of Pharmacy Gadjah Mada University

ABSTRACT

One requirement of semisolid dosage forms that applied to open wound is sterile. Sterilization commonly used is dry and wet sterilization. The objective of this research was to search the influence of dry and wet heat in sterilization process to the change of physical properties of gel base obtained. In wet heat sterilization, gel base was sterilized with autoclave at 115 °C for 30 minutes. In dry heat sterilization, CMC Na was put on an oven at 160 °C while Ca Alginate at 150 °C, each of them for an hour. Then CMC Na and Ca Alginate were turned into gel base. In addition, gel base without sterilization is made as comparison. The next day, the physical properties i.e. viscosity and spreadability of the gel bases were measured. The influence of wet heat to viscosity and spreadability is compared to that if dry heat. The influence is shown by the change of viscosity and spreadability of the gel base to the gel base without sterilization process. The result showed that dry heat had bigger influence to viscosity and spreadability of gel base than wet heat. In wet heat, the gel viscosity decreased to 4,17 dPaS and 23,33 dPaS in dry heat at high level of the mixture of CMC Na and Ca Alginate. The same result emerges at intermediate and low level of the mixture. In wet heat, gel speadability increased to 0,0123 g.cm/sec and 0,1846 g.cm/sec in dry heat at high level of the mixture of CMC Na and Ca Alginate. The same result emerges at intermediate and low level of the mixture.
Keyword: dry heat, wet heat, CMC-Na, Ca-Alginate, physical properties

INTRODUCTION

Hydrogels are three dimensional network that are formed by physically and chemically crosslink of polymer in water. Hydrogels have to be sterile before being applied to open wound (Moyhan and Crean, 2009; Adel, et al, 2010)

Sodium Carboxymethylcellulose (CMC Na) is an anionic polymer available at various grades that differ in degree of substitution and molecular weight (Zatz and Kushla, 1996). Figure 1 shows an ideal CMC Na structure that has 1 degree of substitution. Water molecule at any temperatures can not force the chain to hydrate them. It explains that CMC is water insoluble (Hoefler, 2011)

CMC Na can be sterilized in the dry state by maintaining it at temperature of 160 °C for 1 hour. This process results significant decrease in viscosity of the solution prepared from sterilized material. Aqueous solution of CMC Na may be sterilized by autoclaving. This process reduces the viscosity of the CMC Na solution for about 25%. However, this reduction of viscosity is less than CMC Na solution prepared from material sterilized in the dry state (Rowe et al, 2006)

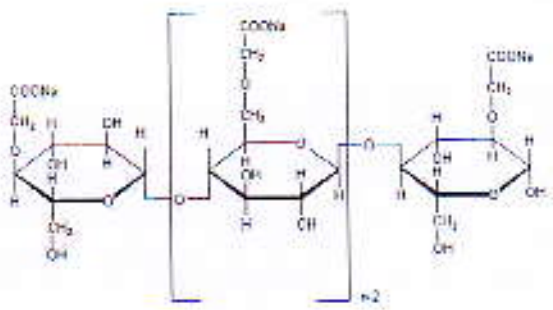

Figure1. CMC Na Stucture

Alginate is a polysaccharide that contains of several units (typically 100 -3000) monomer linked together in flexible chain. Alginate is linear co-polymer of α-L-guluronate dan α-D-mannuronate. Its gelling properties are derived from the binding of Ca ions localized between homopolymeric blocks of guluronate residues (Funduenu et al, 1999). Ca Alginate may be sterilized by autoclaving at 115 °C for 30 minutes or dry heat at 150 °C for 1 hour (Rowe et al, 2006).

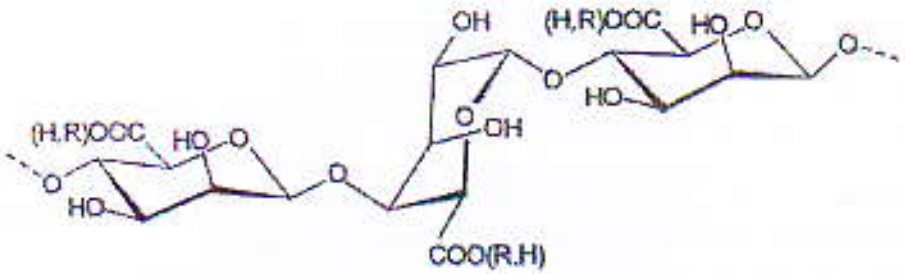

Figure 2. Alginate structure.

METHODOLOGY

Preparation of hydrogel base

R/	Carbopol 941	0.75		
	CMC Na	0.5		
	Ca Alginate	1.0		
	Triethanolamine1		Glycerol	12.5
	water ad	100		

Table 1. Mixture of CMC-Na and Ca-Alginate at various level

level	CMC-Na (g)	Ca-Alginate (g)
High	0.2	0.5
Intermediate	0.5	1.0
Low	0.8	1.5

On dry heat sterilization. CMC Na is put in an oven at 160 °C for an hour while Ca Alginate at 150° C, each of them for an hour. In the aseptic room, CMC Na is poured to aqua p.i and stirred with mixer at 400 rpm for 10 minutes. It is added with Ca Alginate, stirred for 10 minutes at 400 rpm also. Then, it is added with sterilized solution mixture of TEA, Glycerol, and Carbopol, stirred for 10 minutes at 400 rpm. Then, the physical properties of the gel base are determined.

On wet heat sterilization. CMC Na is poured to water and stirred with mixer at 400 rpm for 10 minutes. It is added with Ca Alginate and stirred for 10 minutes at 400 rpm. Then, it is added with Glycerol and Carbopol, stirred until it becomes homogeneous. Then, it is added with TEA. It is sterilized with autoclave 115 °C for 30 minutes. Then, the physical properties of the gel base are determined.

Determination of physical properties

Viscosity determination. Gel base is put in to a container. Then, the portable viscometer is put in the container. Viscosity is obtained by monitoring the moving of the viscosity pointer.

Spreadability determination. The gel base weights 2 g is put in the middle of the ground glass slide. The gel is sandwiched between two ground glass slides. A 1 kg weight is placed on the top of the two slides for 3 minutes. The top slide is subjected to pull of the 80 g. The time and the distant needed to separate the two slides are noted. Spreadability is then calculated using the following formula S = M x L / T.

Where, S = is speadability, M = is the weight in the pan (tied to the upper slide), L = is the length moved by the glass slide, and T = represent the time to separate the slide completely from each other.

RESULTS AND DISCUSSIONS

One requirement of semisolid dosage forms that applied to open wound is sterile. Sterilization process commonly used is wet sterilization. Wet sterilization using autoclave decreases viscosity of the gel base (Rowe et al, 2006). Decreasing of viscosity may be caused by depolimerization of polymer at wet sterilization process. During wet sterilization process hydrolysis may occur. It causes depolymerization occur. On the dry sterilization, depolymerization may be caused by oxidation process. It is interesting to study the phenomena happened during sterilization process that influences physical properties of gel base. The objective of this study is to search the influence of wet heat and dry heat during sterilization process to the physical properties of the gel base containing CMC Na and Ca Alginate. Physical properties studied are viscosity and spreadability. This study is applied to three levels of the mixtures of CMC Na and Ca Alginate, i.e. high, intermediate and low levels.

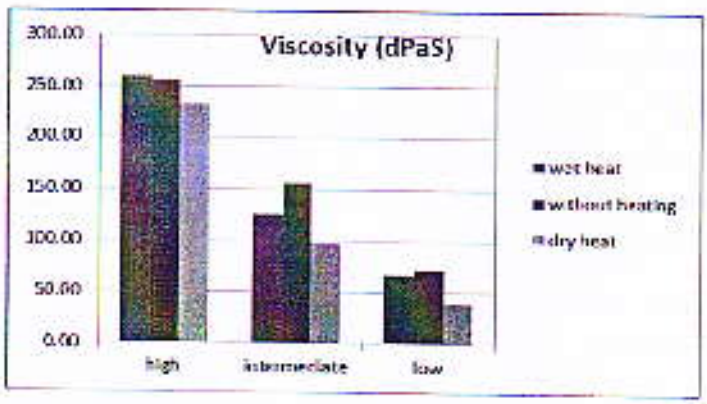

Figure 3. Viscosity of hydrogel base

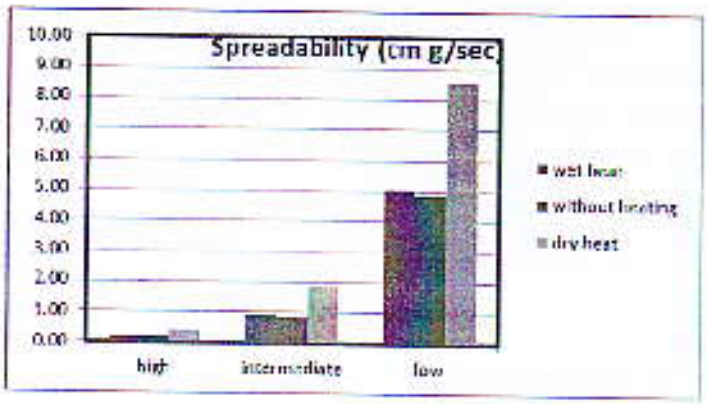

Figure 4. Spreadability of hydrogel base

The influence of the sterilization heat to gel base physical properties is shown by the change of viscosity and spreadability of the gel base. The changes of gel base viscosity sterilized by wet heat are less than that sterilized by dry heat (figure 3). Similar result shown in the speadability properties. The changes of gel base spreadability sterilized by wet heat are less than that sterilized by dry heat (figure 4). In other word, wet heat sterilization has smaller influence to the viscosity and spreadability of gel base than dry heat sterilization. The same result emerges at high, intermediate and low level of the mixture.

Table 2. Viscosity and spreadability of gel base

Lvel	Heat	Viscosity	Change of viscosity	spreadability	Change of spreadability
High	Wet heat	260.00±12.25	4.17	0.2046±0.00145	0.0123
	Dry heat	232.50±8.22	23.33	0.3919±0.0600	0.1846
	Without heat	255.83±10.21		0.2073±0.0104	
intermediate	Wet heat	125.83±3.76	30.83	0.9018±0.0512	0.4114
	Dry heat	97.50±2.24	59.17	1.8435±0.2391	1.0102
	Without heat	156.67±2.58		0.8333±0.0433	
low	Wet heat	67.92±2.46	4.17	5.0672±0.2686	0.4492
	Dry heat	40.83±3.04	31.25	8.5817±0.6212	3.6974
	Without heat	72.08±2.46		4.8843±0.7019	

Hoefler (2011) said that raising or lowering the CMC Na solution temperature has no permanent effect to the viscosity properties. Depolymerization of CMC Na occur when the solution is flattened extremely high temperature for long time heating. Depolymerization causes decreasing viscosity of the gel base. The temperature of the wet heat sterilization is not high enough to degrade the cellulose.

To form a gel, Alginates must contain a sufficient level of guluronate monomer in a block to react with Calcium. The gel properties of Alginate are derived from the interaction between Calcium ion and guluronate blocks. Serp (2002) said that temperature and duration of thermal treatment of Alginate gels influence the polysaccharide network.

On the dry heat sterilization, temperature (160 °C) and duration of thermal treatment (60 minutes) have higher value than wet heat sterilization process (115 °C, 30 minutes). Therefore, the possibility of depolimerization of CMC Na is bigger on dry heat than on wet heat sterilization. It is proven by the fact that the decreasing of viscosity and the increasing of spreadability of gel base sterilized by dry heat is bigger than those sterilized by wet heat. On the other hand, the raise of temperature and duration of thermal treatment will decrease the viscosity of the Ca Alginate solution due to rearrangement and leakage of homopolymer blocks of Ca Alginate.

Dry heat sterilization has bigger influence to viscosity and spreadability of gel base than wet heat sterilization. It is because of temperature and duration of thermal treatment on dry heat sterilization have higher value than wet heat sterilization, so that the possibility of depolimerization of CMC Na and Ca Alginate is bigger.

CONCLUSION

Dry heat sterilization has bigger influence to viscosity and spreadability of gel base than wet heat sterilization.

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