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Research Article

Formulation of Chloramphenicol *In situ* Ophthalmic Gels Using Different Matrix Combinations

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ABSTRACT

In situ ophthalmic gel is solution which form a gel when it is placed onto the eyes. It is intended to have a longer contact time in order to improve the response of therapy. In this experiment, *In situ* ophthalmic gels were formulated by using Chloramphenicol 0.5% and matrix combination of either 0.4% Hydroxy Propyl Cellulose (HPC) or 0.2% Hydroxy Propyl Methyl Cellulose (HPMC) with Sodium Alginate 0.4, 0.5 and 0.6%. All formulas were sterilized by autoclave at 115^0C for 30 minutes. Physical evaluation including organoleptic, pH, viscosity, and drug content showed that all formulas fulfilled the ophthalmic gel requirements according to USP and Indonesian Pharmacopoiea. From rheological study, it can be concluded that the gels had pseudoplastic flow. Either matrix combination of HPC or HPMC with sodium alginate were in solution form during storage and formed a gel once contacted with Simulated Tear Fluids (STF) at 37ºC, which reflected eyes condition. Chloramphenicol release from all *in situ* gels formulations showed sustained release profiles, and 80% release of drugs were retarded to four hours. Antibiotic potency tests of ophthalmic *in situ* gels showed that formulation with HPC and sodium alginate matrix (F1, F2 and F3) had potency of 99.22, 98.45, and 96.97% against *Staphylococcus aureus* as well as 96.46, 96.68, and 96.49% against *Pseudomonas aeruginosa*, while that with HPMC and sodium alginate matrix (F4, F5 and F6) had potency of 99.87, 98.45 and 95.58 against *Staphylococcus aureus* as well as 97.66, 95.05 and 94.42% against *Pseudomonas aeruginosa.* It can be concluded that in situ gel system with either HPC or HPMC in combination with sodium alginate provide sustained release of chloramphenicol. Formulation process, including sterilization did not affect antibiotic potency since it remained in the range of potency value requirements.

Keywords: *In situ* ophthalmic gel, Chloramphenicol, HPC, HPMC, Sodium Alginate

INTRODUCTION

Medical dosage form which frequently used for eye infection treatment are eye drops. Even so, batch of eye drops usually have a slow respond time due to tears dilution effect which are able to quickly eliminate the medical solution on the cornea[1]. Eye drop preparation typically has short contact time with eyes which causes low therapeutic response. For that reason, several approaches are then developed in order to formulate dosage form with better and robust release profile once the solution were contacted onto eyes[2,3]. *In situ* gel dosage form is a solution that experienced reversible transitional phase (sol-gel-sol) caused by changes within the polymer due to formation process of complex structure as its response towards the environment[4]. It is a low viscosity solution; which has reversible transition phase (sol-gel-sol) as its response to physiological enviroment[4]. *In situ* ophthalmic gel has been developed to prolong contact time with eyes[5]. Generally, polymer is used to maintain drug release and prolong its time period. One type of polymer that is used as gelling agent is cellulose derivatives. Hydroxyl propylcellulose (HPC) and hydroxyl propyl methylcellulose (HPMC) are the most preferable of that type[5]. For *In situ* gel dosage form, Sodium alginate which is able to form a gel with calcium, one of the ions within the tears, can also be used[6,7]. Sodium alginate can also be used as matrix; it has structure that is able to form complex structure with calcium ion in tear fluid, resulting in gel formation[8,9]. Pathogen microorganisms, especially bacteria, are able to grow inside the eyes causing infection. The bacteria often to cause the infection are *Staphylococcus aureus, Pseudomonas aeruginosa,* and *Escherichia coli*. Chloramphenicol is an antibiotic with a wide spectrum that is able to deal with severe conjunctivitis in the eye, which was caused by the microorganism[10,11]. It is widely used to treat eyes conjunctivitis. Eye drop preparations are commonly sterilized in high temperature. However, antibiotics activity decreases if it has undergone hydrolysis, chemically (acid), physically (heating), and enzymatically. As a standard to overcome doubts about the possible loss of antibiotic activity (potency) towards its microbial resistance effect, it is necessary to do potential test of the drug after it is produced into pharmaceutical dosage forms. First study on formulation using only cellulose derivate as polymer matrix showed that in order to give prolonged drug release, high polymer level should be applied which in the end give high viscosity of gel, resulting poor flow property during application. The use of sodium alginate in

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