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Influence of Soluble Fillers in Improving Porosity of Handmade Antibiotic-Impregnated Polymethyl Methacrylate (PMMA) Beads: An *in-vitro* Study

Rasyid HN*, PhD, **Soegijoko S**,** PhD

*Department of Orthopaedics and Traumatology, Faculty of Medicine Universitas Padjadjaran / Dr. Hasan Sadikin General Hospital, Bandung, Indonesia

**Biomedical Engineering Program, School of Electrical Engineering and Informatics, Institut Teknologi Bandung, Indonesia

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ABSTRACT

There have been many investigations on non-biodegradable materials acting as an antibiotic carrier for local drug delivery systems based on polymethyl methacrylate (PMMA) beads. However, the material is non-degradable and non-porous so that less than 5% of the encapsulated drug is released. In order to obtain better release of the antibiotics, greater porosity of the beads would be required. Adding fillers could increase the bead's porosity, thus improving the antibiotic release from the beads. The purpose of the study is to optimize release kinetics of gentamicin from handmade beads by adding fillers such as glycine and sodium chloride in different concentrations. Terms of percolation theory will qualitatively be applied in interpreting the final results. Model beads were made by blending the antibiotics (gentamicin) with powdered PMMA, prepared with the inclusion of glycine and different concentration of sodium chloride in 100% monomer. To determine the gentamicin release, beads were placed in phosphate buffered saline (PBS) and aliquots were taken at designated times to measure the gentamicin concentration. Addition of glycine yielded 16 % release of the total amount of gentamicin incorporated in 24 hours. Subsequent addition of sodium chloride resulted in an increased gentamicin release, with little or no difference in gentamicin release once 16 g or more sodium chloride was added (gentamicin release 100% of the amount incorporated). In conclusion, addition of glycine and sodium chloride resulted in an increased release of gentamicin; however, the combination without sodium chloride seemed to have an inhibitory effect on the gentamicin release.

Key Words:
Drug delivery system, gentamicin, PMMA, soluble fillers, glycine, sodium chloride

INTRODUCTION

It is a well established practice in orthopaedic surgery to blend antibiotics into beads of bone cement in the management of musculoskeletal infection. Substantial progress in treating these diseases has been made by the invention of antibiotic-loaded polymethylmethacrylate (PMMA) beads providing the carrier for local delivery of antibiotics in the treatment of infection in orthopaedic practice, such as chronic osteomyelitis [1].

Studies have been conducted to identify any substances that can increase the porosities of the antibiotic beads but have not yielded optimal results. Therefore, further investigation is needed and sodium chloride, which has a larger particle size than glycine particle size, was chosen as filler and its effect evaluated in creating porosity.

Antibiotic release from bone cement is a complex process and important variables include: type of antibiotic, type of bone cement and the mixing conditions [2-4]. Due to the controlled pharmacokinetics, the antibiotic is released from bone cement beads by way of diffusion, which is dependent on the material properties of the beads.

Release of antibiotics is also strongly influenced by the mixing technique. This study used antibiotic powder and soluble fillers. First, PMMA powder is mixed together, monomer methacrylate is then added, allowed to moisturise and again blended using spatula for two minutes to obtain a free flowing soft paste. This leaves intact as many large crystals as possible to create more porous mixture to increase antibiotic elution rate. The PMMA matrix is structured to provide optimum interaction between the carrier matrix and the antibiotic [4]. Initially however, antibiotics adhering to the surface of the PMMA beads will dissolve rapidly to create a so-called burst-release, which is followed by prolonged

Corresponding Author: Hermawan Nagar Rasyid, Dr. Hasan Sadikin Hospital, Faculty of Medicine Universitas Padjadjaran, Bandung, West Java Indonesia
Email: renaldi.prasetia@gmail.com