

# Concepts for increasing gentamicin release from handmade bone cement beads

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**Background and purpose** Commercial gentamicin-loaded bone cement beads (Septopal) constitute an effective delivery system for local antibiotic therapy. These beads are not available in all parts of the world, and are too expensive for frequent use in others. Thus, orthopedic surgeons worldwide make antibiotic-loaded beads themselves. However, these beads are usually not as effective as the commercial beads because of inadequate release kinetics. Our purpose was to develop a simple, cheap, and effective formulation to prepare gentamicin-loaded beads with release properties and antibacterial efficacy similar to the commercially ones.

**Methods** Acrylic beads were prepared with variable monomer content: 100% (500 µL/g polymer), 75%, and 50% to increase gentamicin release through creation of a less dense polymer matrix. Using the optimal monomer content, different gel-forming polymeric fillers were added to enhance the permeation of fluids into the beads. Polyvinylpyrrolidone (PVP) 17 was selected as a suitable filler; its concentration was varied and the antibiotic release and antibacterial efficacy of these beads were compared with the corresponding properties of the commercial ones.

**Results** Gentamicin release rate and the extent of release from beads prepared with 50% monomer increased when the PVP17 content was increased. Beads with 15 w/w% PVP17 released 87% of their antibiotic content. This is substantially more than the gentamicin release from Septopal beads (59%). Acrylic beads with 15 w/w% PVP17 reduced bacterial growth by up to 93%, which is similar to the antibacterial properties of the commercial ones.

**Interpretation** A simple, cheap, and effective formulation and preparation process has been described for hand-made gentamicin-releasing acrylic beads, with better release kinetics and with antibacterial efficacy similar to that of the commercial ones.

In Europe, commercially available gentamicin-loaded polymethylmethacrylate beads (Septopal) constitute an effective delivery system for local antibiotic therapy for osteomyelitis (Bucholz and Engelbrecht 1970, Blaha et al. 1990, Klemm 1993), in combination with systemically delivered antibiotics and surgical debridement. The gentamicin concentrations reached at the site of infection are far higher using antibiotic-loaded bone cement beads than the concentrations achieved by systemic administration of the same antibiotic (Buchholz and Engelbrecht 1970), and far above the minimal inhibitory concentrations of most common pathogens (Wahlig et al. 1978). The use of antibiotic-loaded bone cement beads also gives very low antibiotic concentrations in serum and urine, thereby preventing toxic side effects (Diefenbeck et al. 2006). Alternatives to PMMA beads have been investigated, such as plaster of Paris beads (Dacquet et al. 1992, Bowyer and Cumberland 1994, Gaasbeek et al. 2005). Plaster of Paris is cheaper than bone cement and readily available, and small quantities can be used to make beads containing antibiotic. Plaster of Paris is tolerated when implanted into infected bone cavities, and is it absorbed over a period of weeks to months (Dacquet et al. 1992). Release rates from plaster of Paris beads are higher than from PMMA beads in the first 48 h (Bowyer and Cumberland 1994), but the release rates are much lower than from PMMA beads after this period. Since the PMMA beads work over a longer period of time (about 2 weeks), this paper will concentrate only on PMMA.

Gentamicin-loaded PMMA beads are not, however, commercially available in several parts of the world, including the USA, and they are too expensive for common use in many other countries of the world. Thus, orthopedic surgeons worldwide make antibiotic-loaded beads themselves, sometimes using a template system, but most often by hand-rolling. The antibiotic release kinetics from PMMA bone cements depend