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The influence of vacuum mixing on methylmethacrylate liberation from acrylic cement powder

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Abstract

Polymethylmethacrylate (PMMA) bone cement is a biomaterial used to anchor prostheses during joint replacement surgery. Residual methylmethacrylate monomer (MMA) may be related with the cytotoxic effect of PMMA. The aim of the present paper was to investigate the effect of two different cement mixing methods: hand stirring at atmospheric pressure and under partial vacuum (0.330 and 0.154 bar) on residual monomer liberation in phosphate buffer saline solution from acrylic cement powder. Residual MMA content was determined by high-performance liquid chromatography. Mathematical models were applied to experimental dissolution data revealing that monomer release was significantly reduced in bone cement powder obtained at 0.154 bar vacuum pressure compared to the other mixing conditions. The kinetic models applied are consistent with a simple diffusion mechanism of the monomer from the polymer matrix.

Keywords: Poly(methylmethacrylate); Methylmethacrylate; Biomaterial; Bone cement; Release model; Vacuum mixing

1. Introduction

In the field of biomaterials, polymethylmethacrylate (PMMA) bone cement is a very versatile material used to anchor prostheses during joint replacement surgery.

Painful, aseptic loosening is the most common problem limiting the long-term success of cemented hip arthroplasties (Williams and McQueen, 1992).

In an attempt to understand a possible cause for prosthetic failure, the authors (Vale et al., 1997), have demonstrated the cytotoxic effect of culture media exposed to PMMA (powder) on human fibroblasts, which was probably due to some PMMA soluble components, like the monomer (methylmethacrylate).

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In further work, Bettencourt et al. (2000), found that methylmethacrylate (MMA) release seems to be a surface phenomena, and that the possible actions of the monomer will mainly be due to the initial loss of non polymerized monomer rather than to further depolymerization of the already polymerized cement.

In the present paper, we study the effect of two different cement mixing methods: hand stirring at atmospheric pressure and under partial vacuum, on monomer liberation in phosphate buffer saline solution (PBS) from acrylic cement powder.

2. Materials and methods

2.1. Materials

CMW 1, orthopaedic bone cement, was obtained from CMW Laboratories (Exeter, UK); acetonitrile, MMA, Na_2HPO_4 and KH_2PO_4 were reagent grade (Merck, Darmstadt, Germany); PBS (without $CaCl_2$ and $MgCl_2$) was from Cansera (Canada).

2.2. Methods of bone cement powder preparation

Bone cement powder obtained by mixing the liquid and powder components at atmospheric pressure (non vacuum sample) was prepared according to the procedure described in Bettencourt et al. (2000).

Mixing by vacuum was performed in a polypropylene bowl using a diaphragm pump (ME 2C version C, Vacuubrand, Germany) and a vacuum controller (CVC 24, Vacuubrand, Germany). Two partial vacuum pressures were tested: 0.330 and 0.154 bar in order to obtain two vacuum bone cement powder samples.

2.3. Study of monomer release in PBS

Each powder sample obtained by a different preparation method (non vacuum; vacuum 0.330 and 0.154 bar) was divided into six aliquots (1.75 g each).

Three of the aliquots were exposed to 25 ml of PBS (in closed plastic flasks) and incubated for 24 h at 37°C. Aliquots of supernatant were collected at 0, 0.5, 1, 2, 4, 6, 8, and 24 h for MMA content determination. The remainder were incubated in PBS for only one hour at 37°C (aliquots of supernatant were collected every 10 min for MMA quantification).

2.4. MMA quantification

The concentration of MMA in the collected samples was determined by high-performance liquid chromatography (HPLC), using a modification of a method described in the United States National Formulary (National Formulary of the United States, 1995). The chromatographic column was a Lichrospher 100 RP-18 (5 μm, Merck, Darmstadt, Germany), the rate flow was adjusted to 1 ml/min, the mobile phase was phosphate buffer fortieth-molar per liter (pH 3)/acetonitrile (70:30) and the detection was by ultraviolet absorption at 205 nm.

3. Results and discussion

In Fig. 1, the release profiles of the monomer from the three formulations are compared, in PBS, during the 24 h of exposure.

In all the experiments, there was a rapid rise in MMA concentration followed by a slower and steady release.

The maximum cumulative amount of monomer released, in PBS, by the three different formulations corresponds to the different values of a given in Table 1.

The a values were obtained by fitting the experimental results of the cumulative amount of MMA released during the 24 h of incubation (Fig. 1) to the equation (Donbrow, 1992):

$$y = a(1 - e^{-k_1 t}) \quad (1)$$

characterized by y (cumulative amount of monomer release with time t), a (maximum cumulative amount of monomer released in PBS) and k_1 (first order release rate constant).

The maximum cumulative amount of monomer released in PBS was compared by Student's t-test for unpaired observations.

Results suggest no difference in the maximum cumulative amount of monomer release from acrylic powder prepared at atmospheric pressure or under 0.330 bar vacuum pressure.

The monomer release was significantly reduced in bone cement powder prepared at 0.154 bar vacuum pressure ($P < 0.001$ was interpreted as statistically significant) comparing with both other two mixing conditions.

Low pressure increases the volatility and diminishes the boiling point of the monomer (Wijn et al., 1975). However, it is probable that a significant increase in the volatility of the residual monomer only occurs when the cement is prepared under vacuum pressure close to 0.154 bar.

In our opinion, this fact explains why the MMA release is lower at the vacuum of 0.154 bar when compared to atmospheric pressure or 0.330 bar.

Furthermore, 1st hour dissolution data were fitted by the equations (Brossard and Woessidjewe, 1990):

$$m = m_0 e^{-k_2 t} \quad (2)$$

and

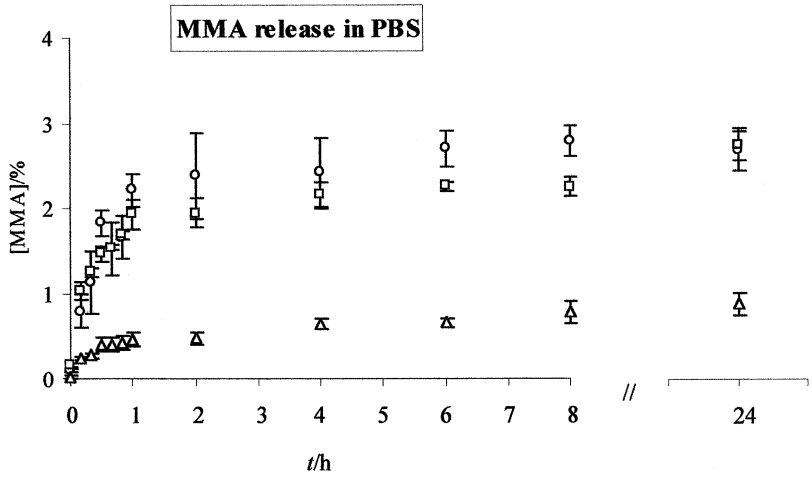

Fig. 1. Experimental dissolution data of monomer release ($\pm$ SD) in PBS: ○, experimental data for MMA release from non vacuum sample; □, experimental data for MMA release from vacuum sample (0.330 bar); △, experimental data for MMA release from vacuum sample (0.154 bar).

Table 1
Parameters resulting from the application of mathematical models to experimental dissolution data, in PBS

Equations	Non vacuum ($p \cong 1.015$ bar)	Vacuum ($p = 0.330$ bar)	Vacuum ($p = 0.154$ bar)
$y = a(1-e^{-k_1 t})$ (24 h)			
$k_1 \pm \sigma(k_1)/\text{min}^{-1}$	0.028 ± 0.004	0.036 ± 0.004	0.020 ± 0.003
$a \pm \sigma(a)/\%$	2.59 ± 0.22	2.22 ± 0.04	0.70 ± 0.08
r	0.98	0.98	0.98
$m = m_0 e^{-k_2 t}$ (Wagner model) (1st hour)			
$k_2 \pm \sigma(k_2)/\text{min}^{-1}$	0.018 ± 0.001	0.024 ± 0.01	0.016 ± 0.003
$m_0 \pm \sigma(m_0)/\%$	2.22 ± 0.05	2.11 ± 0.2	0.74 ± 0.2
r	0.98	0.98	0.98
$Q = k_3 t^{1/2}$ (Higuchi model) (1st hour)			
$k_3 \pm \sigma(k_3)/\%\text{min}^{-1/2}$	0.22 ± 0.008	0.22 ± 0.01	0.058 ± 0.01
r	0.99	0.98	0.98

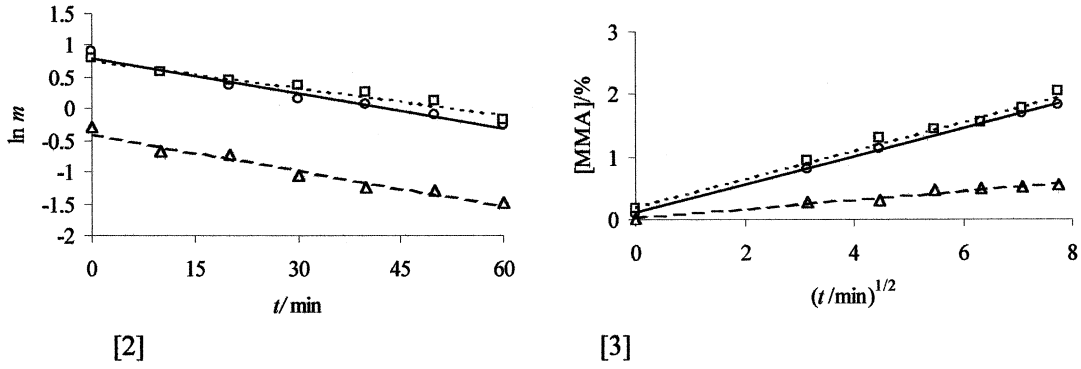

Fig. 2. Application of the mathematical models (2) and (3) to experimental 1st h dissolution data: ○, experimental data for non vacuum sample; – – –, linear fitting for non vacuum sample; □, experimental data for vacuum sample (0.330 bar); — — , linear fitting for vacuum sample (0.330 bar); △, experimental data for vacuum sample (0.154 bar); — — — , linear fitting for vacuum sample (0.154 bar).

$$Q = k_3 t^{1/2} \quad (3)$$

illustrated in Fig. 2.

Eq. (2) (Wagner model) is characterized by m (monomer remaining to be released at time t), m_0 (estimated initial amount of monomer) and k_2 (first order release rate constant). Eq. (3) (Higuchi model) is characterized by Q (cumulative release per unit area after time t) and k_3 (release rate constant related with: diffusion coefficient of monomer in dissolution media, monomer's solubility, monomer's concentration in polymer matrix, porosity and tortuosity).

The application of the Eqs. (2) and (3) to this particular set of data is, as previous explained (Bettencourt et al., 2000), due to the reason that most of the monomer is released within the first hour of incubation.

Parameters resulting from the application of the above mentioned mathematical models (Table 1) show, once again, that the release rate constants and maximum cumulative amount of monomer released are affected only for vacuum value of 0.154 bar. The kinetic models applied show that vacuum mixing technique didn't change the mechanism of monomer release, being in accordance with a surface release phenomena (Bettencourt et al., 2000).

According to Wixson (1992) and Smeds et al. (1997) the vacuum mixing technique is extremely efficient in evacuating air from the cement, getting a more complete reduction in porosity and increasing mechanical properties of bone cement (namely the fatigue life and axial compressive strength). Additionally these systems reduce theatre staff exposure to monomer fumes.

Our study suggest that vacuum will also play an important role in MMA monomer absorbed by the patients but accurate measure of vacuum pressure will be important in order to ensure a minimum MMA liberation.

4. Conclusion

Vacuum mixing technique uses a variety of different chambers. The mixture of the components, in the operating theatre, occurs over the range between approx. 0.340 and 0.150 bar absolute pressure according to Lewis (1997).

The present study indicates that only for vacuum pressures close to 0.150 bar the monomer release will be significantly reduced when compared to the hand stirring in air technique.

As the residual monomer may be related with the cytotoxic effect of PMMA, the preparation of acrylic bone cement under vacuum pressure close to 0.150 bar, will allow a safer application of this biomaterial.

The kinetic models applied are consistent with a simple diffusion mechanism of the monomer from the polymer matrix.

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