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# Optimisation of the composition of an acrylic bone cement: application to relative amounts of the initiator and the activator/co-initiator in Surgical Simplex®P

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**Abstract** In cemented arthroplasties, the two-part self-curing acrylic bone cement is currently the only material used for anchoring the total joint replacement to the contiguous bone. In virtually all commercially available formulations of this cement, the agents used for the initiation and activation/co-initiation of the radical polymerisation reaction are benzoyl peroxide (BPO) and N, N dimethyl-para-toluidine (DMPT), respectively. There are no reports in the open literature on the rationale for the amounts of these and other constituents in the formulations of the cement. Given the concerns that have been raised in the literature regarding the effect of residual DMPT on the body, it is important to keep the starting amounts of BPO and DMPT as high and as low, respectively, as possible. In the present work, the focus is on the relative amounts of these two agents in the case of one widely used commercial formulation, Surgical Simplex®P. Thirty variants of this cement were formulated, covering three concentrations of the co-polymer/BPO (75%, 80%, and 85% of the mass of the powder) and DMPT amounts (ranging from 0.8 %v/v to 2.4% v/v.) The setting time ($t_{set}$), the peak temperature reached during the cement polymerisation process ($T_{max}$), and the ultimate compressive strength (UCS) of each of the formulations were determined in accordance with procedures specified in ISO 5833. A critical examination of all the results indicated that the optimum ratio of the concentration of the initiator (BPO embedded in the PMMA-sytrene co-polymer) to that of the activator/co-initiator (DMPT) in Surgical Simplex®P is 57.14 (80%w/w co-polymer + BPO per 1.4%v/v DMPT). The mean values of $t_{set}$, $T_{max}$, and UCS of this optimum formulation were determined to be 12.30 min, 68°C, and 101 MPa, respectively, all of which are within the limits specified in ISO 5833. The commercially available formulation of this cement contains 2.5%v/v DMPT, while the optimum formulation, as found in the present work, has 44% less DMPT, which may translate to a smaller amount of residual DMPT that is available for elution into the periprosthetic tissue in a cemented arthroplasty, over the *in vivo* life of the joint replacement.

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## 1. Introduction

In orthopaedics, self-curing acrylic bone cement (ABC) is widely used for anchoring endoprostheses to the contiguous bone in cemented arthroplasties. In this application, the primary roles of the cement mantle are to transfer body weight and service loads from the prosthesis to the bone and to increase the load-carrying capacity of the prosthesis-acrylic bone cement-contiguous bone system. There are at least 70 different commercially available ABC formulations on the market today [1]. In terms of composition, there are many similarities and differences between these formulations [1]. First, all are two-part products, with one part comprising the powder constituents and the other part comprising the liquid monomer constituents. Second, all are chemically based on methyl methacrylate, MMA. Third, the powder constituents are pre-polymerised poly (methyl methacrylate) [PMMA] beads, an initiator (benzoyl peroxide, BPO), and a radiopacifier, while the liquid monomer consists of MMA, an activator/co-initiator (N, N-dimethyl-para-toluidine, DMPT)

[except in the case of one brand, Duracem$^{TM}$3, in which 2-(4-(dimethylamino)phenyl)ethanol is used], and a stabilizer. Fourth, the hardened cement is obtained through an exothermic polymerisation reaction when the powder and liquid monomer are mixed. The differences are in a) the composition of the pre-polymerized beads in the powder [PMMA alone or with co-polymer(s)], b) the method of incorporation of the initiator (either contained in the powder beads or present as a discrete entity), c) the presence or absence of contrast agents, antibiotics, stabilizers, plasticizers and reinforcing agents, and d) the relative amounts of the powder and the liquid monomer. The BPO, DMPT, and hydroquinone serve as the initiator (or inducer), activator (or accelerator)/co-initiator, and stabilizer (or inhibitor) of the polymerisation process, respectively. When the BPO and the DMPT are mixed at room temperature, radicals are produced (in a process that is the basis of the decomposition of the BPO by the DMPT), which start the polymerisation process. In other words, these radicals induce the formation of a large amount of high-molecular-weight (at least $10^5$ g/mol) polymer chains (by the radicals attaching themselves to the C=C bond in the MMA) at a very high speed [2]. The hydroquinone ensures that the polymerization process does not occur prematurely. There are four phases in the polymerization process (mixing, waiting, working, and hardening) during which the viscosity of the curing cement increases rapidly from being a fluid dough (at the beginning of the mixing phase) to being solid (at the end of the hardening phase), while the temperature of the curing cement increases at first very slowly (from ambient level) and then very quickly to reach a peak (when the polymerisation terminates and the liquid monomer is depleted).

Only a small amount (typically, 0.1%) of the DMPT is consumed during polymerisation, with the balance remaining in the cement as monomethyl-p-toluidine [1]. Many concerns have been raised about the toxicity of DMPT, this being a consequence of the fact that DMPT is structurally alert to DNA reactivity, is a chromosome-damaging agent that exhibits a significant clastogenic effect [3], is an inhibitor of protein synthesis [4], and can cause methemoglobinemia [5]. These concerns take on special significance because residual DMPT has been detected in cement mantles of retrieved hip implants, with the concentration ranging from 0.05% when the *in vivo* life was 2.5 yr to 0.71% when it was 10.25 yr [6]. It is unknown what proportion of this residual DMPT was eluted into the periprosthetic tissue.

There are no reports in the open literature on the rationale for the amounts of each of the constituents in commercially available acrylic bone cement formulations. In light of the points raised above, it is particularly important to a have a rational approach for determining the relative amounts of BPO and DMPT. Specifically, the amounts of these two constituents should be such that two sets of criteria are fulfilled simultaneously. First, the efficiency of the polymerisation reaction is not compromised. Second, there is no deleterious effect on any of the properties of the curing and cured cement. We herein designate the ratio of the amount of BPO to that of DMPT, in this ideal case, as the optimum ratio of the concentration of the initiator to that of the activator/co-initiator (ORCIA). Thus, the ORCIA for an ABC could be obtained from a critical examination of the values of an array of cement properties, as a function of the relative amounts of BPO and DMPT. By necessity, the array selected is subjective. However, given the use of ABC—for anchoring cemented arthroplasties—this array must include, as a minimum, setting time ($t_{set}$), peak temperature reached during the polymerisation of the cement dough ($T_{max}$), and the quasi-static compressive strength (UCS). (For any cement formulation, the values of these properties must be within the limits prescribed by international standards, such as ISO 5833 and ASTM F 451-99a [7, 8].)

Although there are literature reports on the effect of the relative amounts of BPO and DMPT on various properties of ABCs [9–13], these studies had limitations, as far as estimation of ORCIA is concerned. First, radiolucent cements were used in three of the studies [9, 11, 12]. Second, either the mechanical properties determined were not for the full range of formulations prepared [9, 10, 12] or no mechanical properties were determined [13]. Thus, at this time, the ORCIA of any ABC is unknown. The objective of the present study was to fill this gap in the knowledge base, with specific reference to an ABC brand that is very widely used in cemented arthroplasties, Surgical Simplex®P (Stryker Howmedica Osteonics, Limerick, Ireland), with the properties determined being $t_{est}$, $T_{max}$, and UCS.

## 2. Materials and methods

### 2.1. Formulations tested

In Surgical Simplex®P cement, the powder consists of 73.5%w/w poly (methyl methacrylate)/ styrene co-polymer, 15.0%w/w pre-polymerised PMMA, 10.0%w/w barium sulphate ($Ba_2SO_4$) and 1.5%w/w BPO, while the liquid monomer consists of 97.5%v/v MMA monomer with 2.5%v/v DMPT, with a small amount (80 ppm) of hydroquinone. The formulations tested in this work were 30 variants of this cement, and were obtained thus. The DMPT content was varied from 0.8%v/v to 2.4%v/v. In Surgical Simplex®P, the BPO is incorporated, by the manufacturer, as part of the PMMA-styrene co-polymer in the powder. Thus, the method that was used in the present study to increase the BPO content of the formulations tested was to increase the co-polymer content at the expense of the pre-polymerised

PMMA content. The amounts of DMPT, co-polymer + BPO, PMMA beads, and $Ba_2SO_4$ in each of the formulations tested are presented in Table I. (All the materials used in making the formulations were obtained from Stryker Howmedica Osteonics.)

For all formulations, test specimens were prepared by mixing 40 g of the powder and 20 mL of the liquid monomer manually in a bowl that was open to laboratory ambient conditions (23 ± 1°C; 55 ± 6% relative humidity).

### 2.2. Tests performed

$t_{est}$ and $T_{max}$ were determined for the curing cement, with all experimental steps and data treatment methods being as specified in ISO 5833 [7]. The equipment used was a thermocouple alongside a temperature-time recorder (Eurotherm Chessel Recorder, Model #4102c; Eurotherm, Dublin, Ireland). For each formulation, the test was run in duplicate.

UCS was determined using all the steps and data treatment procedures specified in ISO 5833 [7]. Thus, the cement was poured into a mold comprising 5 holes (each being solid cylindrical in cross-section, with nominal diameter and height of 5.0 ± 0.1 mm and 12.0 ± 0.1 mm, respectively). The resulting solid cylindrical hardened cement specimens were cured in ambient laboratory conditions for 24 ± 2 h, prior to testing on a servohydraulic universal materials testing machine (Model 111, Instron, Inc., High Wycombe, UK), at a crosshead displacement speed of 20 mm/min. For each formulation, five specimens were tested.

## 3. Results and discussion

The whole collection of the $t_{est}$, $T_{max}$ and UCS results are given in Table I and Fig. 1, Table II and Fig. 2, and Table III and Fig. 3, respectively. (Note that mean ± standard deviation values are shown only on Fig. 3 because the tests for $t_{set}$ and

**Table 1** Mean values of the setting times ($t_{set}$) of the formulations

| DMPT (%v/v) | $t_{set}$ (min) 75%w/w co-polymer[a] | 80%w/w co-polymer[b] | 85%w/w co-polymer[c] |
|---|---|---|---|
| 0.8 | 17.15 | 15.40 | 17.40 |
| 0.9 | 14.90 | 15.40 | 15.30 |
| 1.0 | 14.55 | 14.80 | 15.30 |
| 1.2 | 14.35 | 14.30 | 15.40 |
| 1.4 | 13.15 | 12.30 | 14.00 |
| 1.6 | 12.10 | 14.70 | 13.80 |
| 1.8 | 12.60 | 14.50 | 13.80 |
| 2.0 | 12.65 | 13.60 | 13.90 |
| 2.2 | 12.20 | 13.80 | 13.90 |
| 2.4 | 11.20 | 12.80 | 12.30 |

[a]The powder contained 30.0 g of MMA-styrene co-polymer + BPO, 6.0 g of PMMA beads, and 4.0 g of $BaSO_4$.

[b]The powder contained 32.0 g of MMA-styrene co-polymer + BPO, 4.0 g of PMMA beads, and 4.0 g of $BaSO_4$.

[c]The powder contained 34.0 g of MMA-styrene co-polymer + BPO, 2.0 g of PMMA beads, and 4.0 g of $BaSO_4$.

**Table 2** Mean values of the peak temperature reached during the polymerization ($T_{max}$) of the formulations

| DMPT (%v/v) | $T_{max}$ (°C) 75%w/w copolymer | 80%w/w copolymer | 85%w/w copolymer |
|---|---|---|---|
| 0.8 | 66 | 60 | 46 |
| 0.9 | 73 | 60 | 47 |
| 1.0 | 69 | 58 | 61 |
| 1.2 | 80 | 64 | 58 |
| 1.4 | 76 | 68 | 49 |
| 1.6 | 70 | 72 | 62 |
| 1.8 | 65 | 72 | 67 |
| 2.0 | 77 | 58 | 53 |
| 2.2 | 70 | 75 | 64 |
| 2.4 | 71 | 64 | 61 |

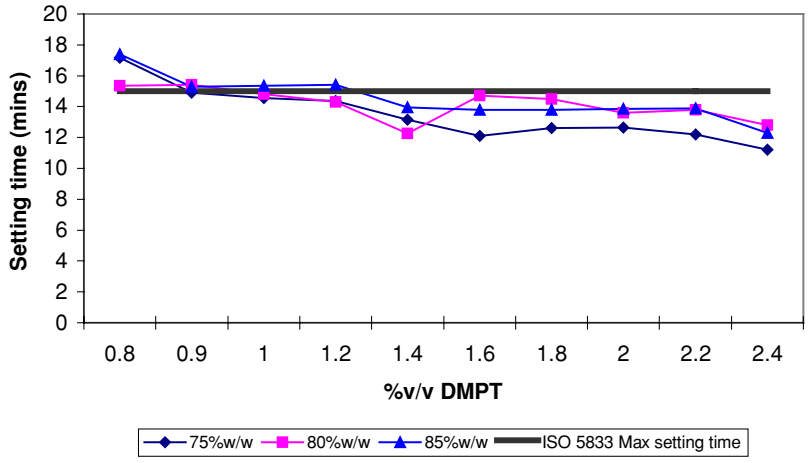


**Fig. 1** Mean values of $t_{set}$ of the formulations.

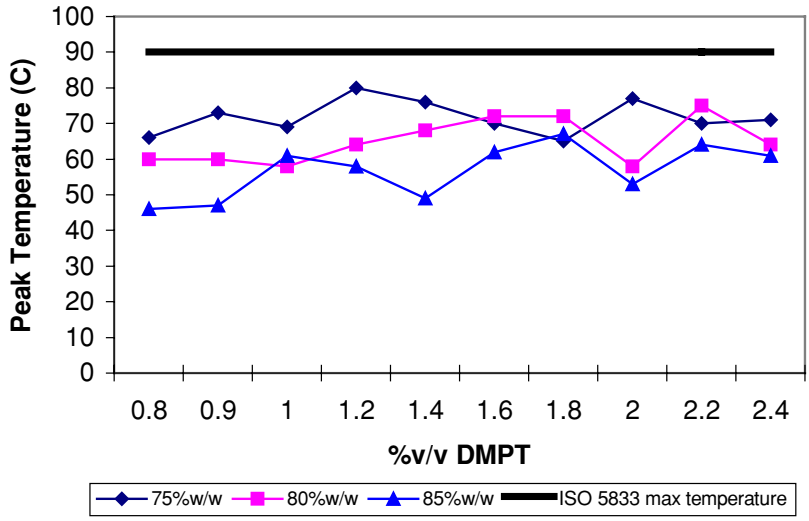


**Fig. 2** Mean values of $T_{max}$ of the formulations.

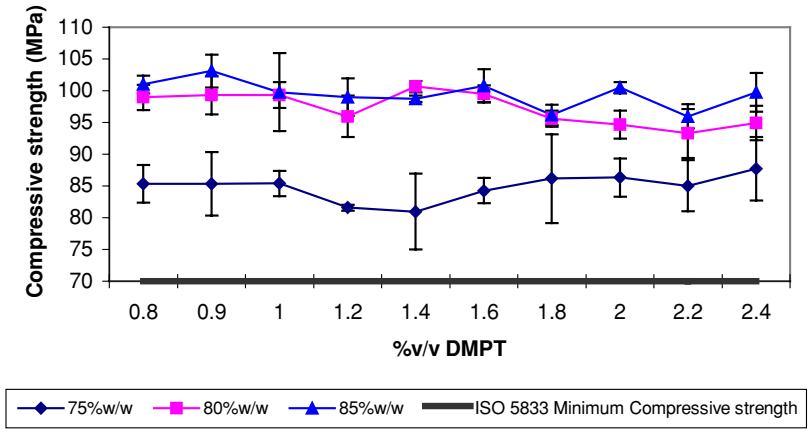


**Fig. 3** Mean values of UCS of the cements.

**Table 3** Mean values of the ultimate compressive strength (UCS) of the cements

| | UCS (MPs) | | |
|---|---|---|---|
| DMPT (%v/v) | 75%w/w copolymer | 80%w/w copolymer | 85%w/w copolymer |
| 0.8 | 85.3 | 89.5 | 101.1 |
| 0.9 | 85.3 | 99.3 | 103.1 |
| 1.0 | 85.4 | 99.3 | 99.8 |
| 1.2 | 81.6 | 96.0 | 99.0 |
| 1.4 | 81.0 | 100.7 | 98.7 |
| 1.6 | 84.3 | 99.5 | 100.8 |
| 1.8 | 86.2 | 95.6 | 96.2 |
| 2.0 | 86.3 | 94.7 | 100.5 |
| 2.2 | 85.0 | 93.3 | 96.0 |
| 2.4 | 87.7 | 94.9 | 99.7 |

$T_{max}$ were run in duplicate, whereas the tests for UCS were run on five specimens.)

From these results, it is seen that for all formulations, the values of the properties determined were within the ISO 5833 limits, except for $t_{set}$ for seven formulations (Fig. 1). It is desirable that an orthopaedic acrylic bone cement has a moderate value of $t_{set}$ (so that the cement does not cure too fast or too slowly), a low value of $T_{max}$ (so that the potential for thermal necrosis of the periprosthetic tissue, during the setting of the cement dough in the bone bed during a joint replacement, is low), and a high value of UCS (so that the cured cement mantle in the arthroplasty can withstand high compressive loads imposed on it during normal daily activities). When the present results are reviewed, *vis a vis* the above mentioned points, it appears that ORCIA for Surgical Simplex®P is 57.14 (80%w/w co-polymer + BPO per 1.4%v/v of DMPT).

Pascual *et al.* [9] reported on the effect of the relative amounts of BPO (0.75, 1.25, and 2.00%w/w) and DMPT (1.00 and 2.00%v/v) on $t_{set}$, $T_{max}$, and UCS of an acrylic bone cement. However, in that study, the formulations were based on a radiolucent cement, and UCS was determined for only six of the twenty nine formulations prepared. In the study by Vazquez *et al.* [10], radiopaque cement was used, but the properties determined ($t_{set}$, doughing time, $T_{max}$, ultimate tensile strength, tensile modulus, and tensile strain to fracture) were for four formulations (0, 6.25, 12.50, and 18.75%

w/w $BaSO_4$) that contained the same amount of BPO (1.5% w/w) and DMPT (0.82% w/w). Hasenwinkel *et al*. [11, 12] reported on the effect of relative amounts of BPO (0.50, 1.25, 2.00, 2.75 g per 100 mL of MMA) and DMPT (0.2, 1.4, and 4.9 mL per 100 mL of MMA) on $T_{max}$, residual monomer content, three-point flexural strength, three-point flexural modulus, fracture toughness, and fatigue performance of a two-solution acrylic bone cement. (A two-solution cement is one in which the PMMA powder is pre-dissolved into the MMA, and the BPO is added to one solution while the DMPT is added to the other solution.) However, in these studies [11, 12], the formulations were based on a radiolucent cement, and, in the case of the fatigue tests, results were presented for only three of the twelve formulations prepared [12]. The study by Milner [13] was on fifteen formulations of a radiopaque bone cement (BPO concentrations of 0.75, 1.00, and 1.50%w/w and DMPT concentrations of 0.50, 0.75, 1.00, and 2.00%w/w). However, in that study, no mechanical property values were determined, the only results given being those for $t_{set}$ and $T_{max}$. Thus, it is seen that, from the perspective of obtaining ORCIA, the results from the five relevant literature reports [9–13] cannot, strictly speaking, be compared to those in the present study.

The limitation of the present study is that a number of important properties of the formulations (such as powder particle distribution, polymeric structure, and powder polydispersity index, PDI) and of the cement (such as fatigue life and residual monomer content) were not determined. For three reasons, this limitation does not affect the underpinning of the present work. First, explanations for the trends seen in the results (for which data like powder PDI are important) were outside the ambit of the present study. Second, the properties that were determined in the present work are very important —$t_{set}$ is a key parameter as far as the handling of the cement is concerned, $T_{max}$ is an index of the potential for thermal necrosis of the periprosthetic tissue, while UCS gives an indication of the ability of the cement mantle to resist compressive loading, which is a common mode of loading of the arthroplasty during a host of normal daily activities. Third, the present study was designed to illustrate a rational approach to determining the composition of an ABC. In future work, other properties (such as those mentioned above) would be determined, which should allow the case for the ORCIA estimated in the present study to be strengthened.

## 4. Conclusion

The optimum ratio of the concentration of the initiator (BPO embedded in the PMMA-sytrene copolymer) to that of the activator/co-initiator (DMPT) in Surgical Simplex®P acrylic bone cement was determined to be 57.14 (80%w/w co-polymer + BPO per 1.4%v/v DMPT). The mean values of the setting time, the peak temperature reached during the polymerisation process, and the ultimate compressive strength of this optimum formulation were determined to be 12.30 min, 68°C, and 101 MPa, respectively, all of which are within the limits specified in ISO 5833. The commercial formulation of this cement contains 2.5%v/v DMPT; thus, the formulation with the optimum composition, as found in the present work, has 44% less DMPT which may translate to a smaller amount of residual DMPT that is available for elution into the periprosthetic tissue in a cemented arthroplasty, over the *in vivo* life of the joint replacement.

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## References

1. K-D KUHN, "Bone Cements: up to date comparison of physical and chemical properties of commercial materials" (Springer-Verlag, Germany, 2000).
2. F. W. BILLMEYER, "Textbook of Polymer Science", 2nd ed. (John Wiley & Sons, New York, 1971).
3. M. TANNINGHER, R. PASQUINI and S. BONATTI, *Environ. Mol. Mutagen.* **21/4** (1993) 349.
4. B. VAZQUEZ, B. LEVENFELD and J. SAN ROMAN, *Polym. Int*. **46** (1998) 241.
5. J. L. POTTER, C. E. KRILL, D. NEAL and W. G. KOFRON, *Ann. Emerg. Med*. **17/10** (1988) 1098.
6. P. BOESCH, H. HERMS and F. LINTNER, *Arch. Toxicol.* **51** (1982) 157.
7. ISO 5833, Implants for surgery-Acrylic resin cements (2003).
8. ASTM F 451-99a, Standard specification for acrylic bone cement (2004).
9. B. PASCUAL, B. VAZQUEZ, M. GURRUCHAGA, I. GONI, M. P. GINEBRA, F. J. GIL, J. A. PLANELL, B. LEVENFELD and J. SAN ROMAN, *Biomater*. **17** (1996) 509.
10. B. VAZQUEZ, S. DEB and W. BONFIELD, *J. Mater. Sci.: Mater. Med.* **8** (1997) 455.
11. J. M. HASENWINKEL, E. P. LAUTENSCHLAGER, R. L. WIXSON and J. L. GILBERT, *J. Biomed. Mater. Res.* **47** (1999) 36.
12. J. M. HASENWINKEL, E. P. LAUTENSCHLAGER, R. L. WIXSON and J. L. GILBERT, *J. Biomed. Mater. Res.* **59** (1999) 411.
13. R. MILNER, *J. Biomed. Mater. Res. Part B: Appl. Biomater*. 68B (2004) 180.