

## COMPOSITION INFLUENCE ON PROPERTIES OF ACRYLIC COMPOSITES LOADED WITH SYNTHETIC HYDROXYAPATITE

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**Abstract** -A study of composition influence over some properties of acrylic composites loaded with hydroxyapatite is presented. "Two pastes" method from dental obturants was used to prepare the composites. The working ( $2.5 < t_w < 3.3$  min) and setting ( $2.7 < t_s < 3.7$  min) times was in range reported for acrylic bone cements and enthalpy (around 40-60 kJ/mol) according to reports for acrylic materials. The absorption ( $110-240 \mu\text{g}/\text{mm}^3$ ) and solubility ( $10-130 \mu\text{g}/\text{mm}^3$ ) showed values higher than normalized ranges. Mechanical properties (compression strength and elastic modulus) showed a wide range result, including in some cases, better values than reported by other authors. The drug release from the composites was studied through Baker's treatment which justifies not only diffusion, but the migration and dissolution of drug in the phosphate buffer. The diffusion coefficients ( $10^{-10} \text{cm}^2/\text{s}$ ) and 15-20 % of drug release at 15 days support this result too.

**Keywords** — -composite, copolymer, hydroxyapatite composite, bone regeneration, drug release.

### I. INTRODUCTION

Many composite materials have been developed for biomedical applications. These may include ceramic or polymer matrix composites (Doyel, 1990; Kasuga *et al.*, 1990 and Soltez, 1988). The ceramic material may range from biodegradable, such as bioactive glass (Greish and Brown, 2000) to non biodegradable such as stoichiometric hydroxyapatite,  $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ , HA (Fuentes *et al.*, 2005).

The mechanical properties of composites based on poly(acrylic-co-itaconic) acid reinforced with powder mixtures of bioactive glass and tetracalcium phosphates are enhanced by the quantity of glass. Also, the concentrations of Ca, Si, and P increased with the immersion time on SBF owing to the formation of an apatite layer on their surfaces (Greish and Brown, 2000).

Hydrophilic composite structures are designed to mimic the transport and mechanical properties of natural soft tissue such as tendons, ligaments and intervertebral discs. Systems such as poly (2-hydroxyethyl methacrylate (HEMA)-co-caprolactone (CL)) showed an increase the modulus and maximum strength with the increasing content of PCL and filler of polyethylene terephthalate (PET) fibres (Ambrosio *et al.*, 1998).

Other groups have been proposed a hydroxyapatite-reinforced polymer as a method of improving the bio-

logical properties of bone cements and implants materials. For that, HA was incorporated to polymethyl methacrylate (PMMA) matrix and improved osteoblast response a compared to PMMA alone. This method may be useful to provide PMMA materials with enhanced osteogenic properties (Moursi *et al.*, 2002 and Morejón *et al.*, 2005). On the other hand, a novel composite made from spontaneous precipitation of HA in aqueous suspensions of polymer particles of sulphonated polysulphone was prepared. The time of the precipitation process was allowed to regulate the inorganic content of the composite (Spanos *et al.*, 2002).

Another research group prepared precopomposite structures by combining  $\beta\text{-Ca}_3\text{PO}_4$  ( $\beta$ -tricalcium phosphate or  $\beta$ -TCP) with poly (L-lactic) acid and poly (DLlactic-co-glycolide). The hydrolysis from  $\beta$ -TCP to calcium deficient hydroxyapatite (CDHA,  $\text{Ca}_9(\text{HPO}_4)(\text{PO}_4)_5\text{OH}$ ) was performed at  $56^\circ\text{C}$  -a temperature slightly above the glass transition of the polymers-. The composite obtained with PLGA (85:15) copolymer showed an 85 % of transformation from  $\beta$ -TCP to CDHA in 24 h, although according to FTIR the transformation was completed. The mechanical properties of these hydrophilic copolymers was in the range of 12-14 MPa and the elastic modulus was 2.5-6 GPa. (Durucan and Brown, 2000a; and Durucan and Brown, 2000b).

In an effort to develop a material with mechanical properties more closely approximating those of hard tissues, HA-composites have been selected for study (Ambrosio *et al.*, 1998; Greish and Brown, 2000 and Lewis and Nielsen, 1970).

The aim of the present study was prepared composites with HA load based on a classic dental obturants but with potential application as acrylic bone cement, substituting BisGMA (base monomer) by poly 2hydroxyethyl methacrylate, and silanized quartz by hydroxyapatite. The study of composition influence over the main properties of this new composites comparing with the requirements to use in human implantology was made.

### II. EXPERIMENTAL SECTION

#### A. Preparation and characterization of synthetic hydroxyapatite.

Stoichiometric synthetic hydroxyapatite with Ca/P=1.66 was prepared (Peón *et al.*, 2004). FTIR were recorded in a BOMEN DA3 spectrometer in the  $4000-400 \text{cm}^{-1}$  range using the KBr pellet technique. X-ray powder

pattern was measured in 20-60  $2\theta$  range with a Seifert C-3000 diffractometer, using Cu-K  $\Delta$  radiation (Table 1).

The HA were initially analyzed by IR. The characteristic bands of the  $\nu_2(\text{PO}_4^{3-})$  is observed at 566 and 601  $\text{cm}^{-1}$ ,  $\nu_1(\text{PO}_4^{3-})$  at 954  $\text{cm}^{-1}$ , and the  $\nu_3(\text{PO}_4^{3-})$  to the 1087 and 1022  $\text{cm}^{-1}$ . These reflections indicate the classification of the polyhedrons of  $\text{PO}_4^{3-}$  in the structure of the glass. Besides, at 3566  $\text{cm}^{-1}$  a main vibration  $\nu(\text{OH}^-)$  is observed, joined to bands at 3400 and 1629  $\text{cm}^{-1}$  (H-O-H) from water absorption of synthesis process. The band at 628  $\text{cm}^{-1}$  is attributed to the OH groups (Fowler, 1974).

Table 1. IR bands and X-ray pattern of synthetic HA

IR bands	$\nu^*(\text{cm}^{-1})$	$\nu_{\text{exp}}(\text{cm}^{-1})$	$2\theta^{**}$	$I_r^{**}(\%)$	$2\theta_{\text{exp}}$	$I_{r_{\text{exp}}}(\%)$
$\nu(\text{OH}^-)$	3572	3574	25.90	40	25.85	48.8
$\nu_3(\text{PO}_4^{3-})$	1087	1093	31.80	100	31.75	100
	1046	1041				
$\nu_1(\text{PO}_4^{3-})$	962	957	32.22	60	32.15	71.3
	$\delta(\text{OH})$	630				
$\nu_2(\text{PO}_4^{3-})$	601	601	34.08	25	34.00	28.7
	571	569				
$\nu_4(\text{PO}_4^{3-})$	474	468	39.85	20	39.80	24.3
	H-O-H	3450				
H-O-H	1640	1629	49.51	40	49.50	39.4
$\text{CO}_3^{2-}$	1450	1449	50.54	20	50.50	20.1
	1420	1418				
P-OH	870	871	53.19	20	53.15	20.1
		(874***)				

\*(Fowler *et al.*, 1974), \*\* (ICDD, 1998), \*\*\*  $\text{CO}_3^{2-}$  plane

The HA were initially analyzed by IR. The characteristic bands of the  $\nu_2(\text{PO}_4^{3-})$  is observed at 566 and 601  $\text{cm}^{-1}$ ,  $\nu_1(\text{PO}_4^{3-})$  at 954  $\text{cm}^{-1}$ , and the  $\nu_3(\text{PO}_4^{3-})$  to the 1087 and 1022  $\text{cm}^{-1}$ . These reflections indicate the classification of the polyhedrons of  $\text{PO}_4^{3-}$  in the structure of the glass. Besides, at 3566  $\text{cm}^{-1}$  a main vibration  $\nu(\text{OH}^-)$  is observed, joined to bands at 3400 and 1629  $\text{cm}^{-1}$  (H-O-H) from water absorption of synthesis process. The band at 628  $\text{cm}^{-1}$  is attributed to the OH groups (Fowler, 1974).

The most intense peaks at XRD patterns appear in the range of 20-60°,  $2\theta$ ; characteristic of the apatitic phase (JCPDS # 9-432). The appearance of the characteristic peaks (31.80, 32.22 and 32.93 in  $2\theta$ ) suggests the acceptable crystallinity of the apatitic structure. There is a good agreement between the unit cell parameters ( $a = b = 9.418 \text{ \AA}$ ;  $c = 6.884 \text{ \AA}$ ,  $V = 528.8 \text{ \AA}^3$ ) and the same parameters ( $a = b = 9.412 \text{ \AA}$ ;  $c = 6.886 \text{ \AA}$ ,  $V = 528.3 \text{ \AA}^3$ ) calculated from XRD patterns.

Thermogravimetric (TG) and differential thermal analyses (DTA) were carried out in a Seiko 55C 5200 TG-DTA 320 System under nitrogen flow of 50 mL/min with a heating rate of 5°C/min (Fig. 1). There are no exist any differences during all the temperature range analyzed by TG and DTA because the percent variation was 4 % maximum in TG assigned to a water loss occluded inside the HA particles aggregates. The DTA analysis not shows a signal (peak) that indicates transformation at the hydroxyapatite.

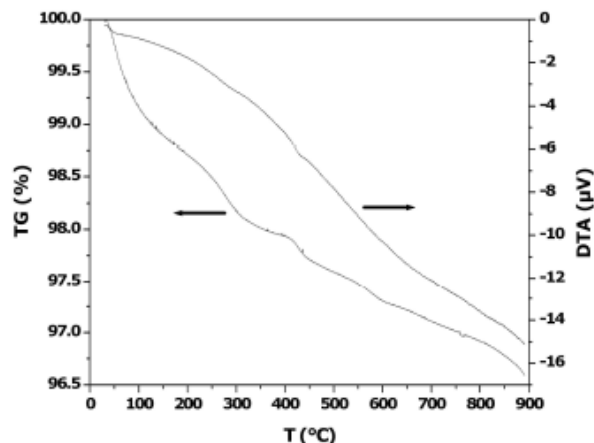


Figure 1. TG and DTA of synthetic hydroxyapatite

### B. TEGDMA/HEMA – HA composites synthesis.

Prior to composite fabrication, the HA was placed in a mortar and ground into a fine powder ( $<160 \mu\text{m}$ ) by breaking up agglomerated particles. The rest of the reactives (chemical degree) were provide by BDH Chemicals Ltd. and was used as received without further purification. Starting from here, for the better comprehension of the formulations and the results, the substances will be recognized by its proper letter.

- tetraethylenglycol dimethacrylate (TEGDMA)  $\rightarrow$  **T**
- 2-hydroxyethyl methacrylate (HEMA) as itself
- hydroxyapatite (HA)  $\rightarrow$  **H**
- benzoyl peroxide (BPO)  $\rightarrow$  **P**
- N,N'-dimethyl-p-toluidine (DMpT)  $\rightarrow$  **M**
- methyqyl ether of hdrouinone QMH  $\rightarrow$  **Q**

The “two pastes” classical method for dental obturants was employed. To prepare the samples, two equal parts of both pastes were mixed in a glass cylinder helped by a spatula (6 mm  $\varnothing$  x 12 mm height) as shown at Fig 2. After the polymerization process at room temperature, the glass mold was broken and samples were washed by immersion in distilled water and dried over heat air by 1 min. The sample was used as obtained, based on requirements to determine mechanical properties (ISO, 2000).

### C. Statistical treatment of the samples.

In order to evaluate the effect of the monomers content in % (use TEGDMA as pivot) (**T**), and the content in % also, of HA load (**H**), initiator (**P**), amine (**M**) and inhibitor (**Q**) on the studied properties, different series were prepared as summarised in Table 2. Q was selected as alias variable and  $\mathbf{Q} = \mathbf{T}^* \mathbf{H}^* \mathbf{P}^* \mathbf{M}$ . H load was range between 20 -25 % because the mixture viscosity prevent the addition of more load. For each set of variables, two pastes, base and catalytic were prepared. Interactions between the different parameters were considered in this experimental design (Almirall *et al.*, 2004). The statistical treatment was made in Statgraphics PLUS v5.1 over Windows through a multilineal polynomial equation type:  $Y = \beta_0 + \beta_T T + \beta_H H + \beta_P P + \beta_M M + \beta_{TH} TH + \beta_{TP} TP + \beta_{TM} TM + \beta_{HP} HP + \beta_{HM} HM + \beta_{PM} PM + \beta_{THP} THP + \beta_{THM} THM + \beta_{TPM} TPM + \beta_{HPM} HPM + \beta_{THPM} THPM$

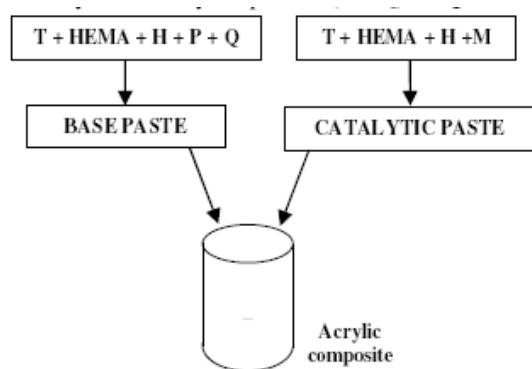


Figure 2. Preparation scheme of composites

Table 2. Experimental design.

Formulación	T	H	P	M	Q
30T20H15P15M10Q	30	20	1.5	1.5	0.10
70T20H15P15M5Q	70	20	1.5	1.5	0.05
30T25H15P15M5Q	30	25	1.5	1.5	0.05
70T25H15P15M10Q	70	25	1.5	1.5	0.10
30T20H20P15M5Q	30	20	2.0	1.5	0.05
70T20H20P15M10Q	70	20	2.0	1.5	0.10
30T25H20P15M10Q	30	25	2.0	1.5	0.10
70T25H20P15M5Q	70	25	2.0	1.5	0.05
30T20H15P20M10Q	30	20	1.5	2.0	0.10
70T20H15P20M5Q	70	20	1.5	2.0	0.05
30T25H15P20M5Q	30	25	1.5	2.0	0.05
70T25H15P20M10Q	70	25	1.5	2.0	0.10
30T20H20P20M5Q	30	20	2.0	2.0	0.05
70T20H20P20M10Q	70	20	2.0	2.0	0.10
30T25H20P20M10Q	30	25	2.0	2.0	0.10
70T25H20P20M5Q	70	25	2.0	2.0	0.05
50T22H17P17M7Q	50	22.5	1.75	1.75	0.075

#### D. Thermoanalytical characterization of composites.

A Mettler TA-300, DSC-30 system of thermal analysis was used to perform measurements, in a dynamic program heat of 5°C/min. Approximately 30 mg of the samples were putted on the aluminum sample pan. The temperature changes were automatically measured with precision of  $\pm 0.01^\circ\text{C}$  while the room temperature was maintained at  $(23 \pm 1)^\circ\text{C}$  and the relative humidity ranging  $(55 \pm 2) \%$ . The working and setting times of the samples was signalised in Fig 3.

The working time ( $t_w$ ) was determined calculating the time from the beginning of assay to the first slope break, where the heat value change. The setting time ( $t_s$ ), was determined calculating the time from the beginning of assay to the maximum heat value. The polymerization enthalpy ( $\Delta H_p$ ), was calculated assuming the area under the curve (Fig 3) (Peón *et al.*, 2004).

#### E. Absorption and solubility studies.

Water sorption and solubility tests were determined according to the method describe in ISO 4049 (ISO, 2000) standards form.

Five cylindrical specimens at least, (15 mm diameter x 1 mm thickness) were prepared into Teflon mould between two glass slides, covered and leave polymerized under self cured process. On removal the specimen were placed in a desiccators containing freshly dried silica gel.

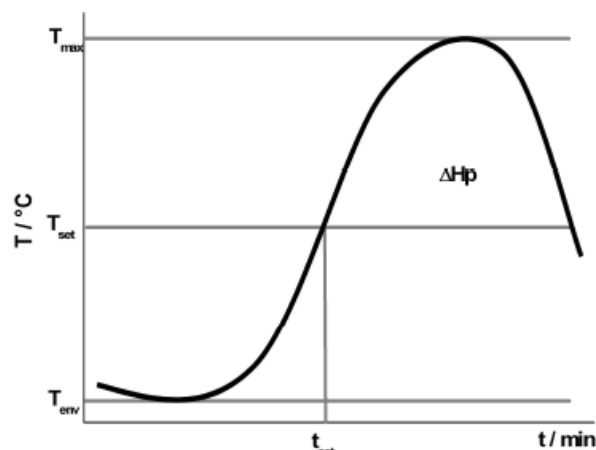


Figure 3. Calculus scheme from thermoanalytical studies

After 22 h they were removed, stored in desiccators at 23°C for 1 h and weighed with a precision of 0.01 mg. This cycle was repeated until a constant mass ( $m_1$ ) was obtained. The discs were immersed in distilled water at 37°C for seven days, the removed, bottled dry and weighed ( $m_2$ ). After this weighing, the specimens were reconditioned to a constant mass ( $m_3$ ) in the desiccators using above describe cycle.

The thickness and diameter of the samples were measured accurately at five points using a micrometer ( $\pm 0.25$  mm) and their measured values were employee in the calculus of volume in  $\text{mm}^3$ . The values of water absorption ( $A$ ) and solubility ( $S$ ) were calculated for each disc using the Eqs. 1 and 2 (Veranes *et al.*, 2006).

$$A = \frac{m_2 - m_3}{V} \quad (1)$$

$$S = \frac{m_1 - m_3}{V} \quad (2)$$

#### F. Mechanical studies

The compression strengths of the composites were determined using a Universal Testing Machine BIONIX MTS 350 (Bionix, USA). The samples were prepared as explained in section 2.2. Five samples at least were tested for each composition according to experimental design (Delgado, 1998; Almirall *et al.*, 2004).

#### G. Drug release from copolymers.

An antibiotic (in powder form) was tested in this study. 20 mg of sodium cefuroxime (Batch 6001, Center for Investigation and Development of Medications, CIDEM, Cuba) by each cylinder sample was previously mixed, divided in two part of 10 mg each one, with liquids monomers, before the addition of hydroxyapatite to form the pastes (see Fig. 2). A calibration curve for cefuroxime at concentrations between 0-50 ppm range regular intervals was prepared completing with phosphate buffer pH = 7.4.

The *in vitro* kinetic studies of the antibiotics release were carried out putting the slabs in 10 mL of phosphate buffer, in a glass tube with tightly closed cover at  $(37 \pm 1)^\circ\text{C}$ . The whole added buffer was extracted and replaced every 90 min for the first day, and every 24 h

until complete 15 days. The calibration curve and the samples were read in quartz recipients of 1 cm optic pass at 262 nm for the cefuroxime in UV-Visible spectrophotometer (Nelson *et al.*, 1992)

### III. RESULTS AND DISCUSSION

#### A. Thermoanalytical studies

All the DSC thermograms showed an endothermic peak related to the heat emission by the polymerization process of the sample (see Fig. 3). In case of working and setting ( $t_{set}$ ) time, the statistical behavior was the same.

The working and setting times behave according with composition and it does not obtain any unexpected results [who reference should be here?17]. The  $t_w$  range oscillated between 2.5-3.3 min, in all cases higher than 1.5 min (90 s). The  $t_s$  range varied between 2.7-3.7 min, less than 5 min reported by dental international norms (ISO, 2000) and acrylic cements, among 3-15 min (ISO, 2002)

$$t_w = 2.84 - 0.07A - 0.06B - 0.15C - 0.21D + 0.05BE \quad (3)$$

The statistical model obtained to working time (Eq. 3) showed with clarity the marked influence of the initiator and amine percent ( $C$  and  $D$  variables). The composition and load have a lower influence ( $A$  and  $B$  variables). However, all factors involved in the study influence on the times analysis. The amine influences three times more than composition. On the other hand, initiator influence twice. Composition and load had same influence.

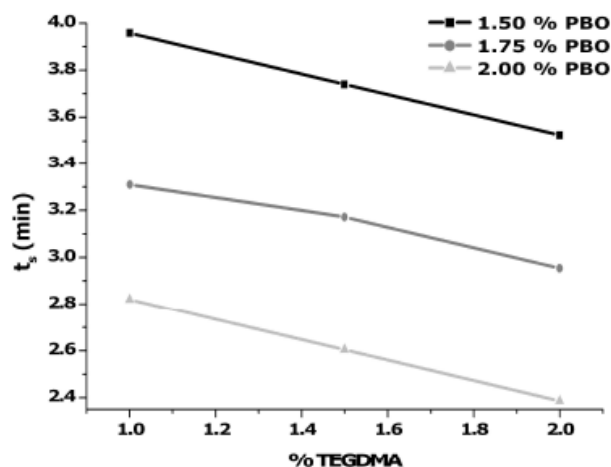


Figure 4. Setting time vs. amine and initiator percent

As it can be seen at Fig. 4, when the amine and initiator percent increase and the setting time diminishes, as it can expect. Obviously, in first stage of the polymerization process, the amine and initiator (radical generators) are very important because their action increase the polymerization rate, and the setting of the composite.

$$t_s = 3.17 - 0.06A - 0.06B - 0.16C - 0.22D \quad (4)$$

Even when composition and load are less influential than amine and initiator percent, it can observe from the Eq. 4 that if it work with the higher quantity of base monomer ( $T$ ) which higher density than HEMA, the more ramify structure of TEGDMA provide a greater

rigidity to composite, and then, a lower working and setting time (Antonucci and Toth, 1985).

The obtained values are inside the established ranges for this type of materials (ISO, 2000), as seen before. The optimal value should be determined by the user's necessity between the normalized values. For example, the  $t_w$  should be the biggest possible, which means more time of preparation and mixture to surgeon. For the same reason the setting time ( $t_s$ ), should be the lowest in order to reduce the surgical time.

When the reaction heat was determined, it is observed an oscillation of the values approximately between 49 and 63 kJ/mol as observes in Table 3. The acrylates has a value of  $\Delta H_p$  oscillates between 40-60 kJ/mol according to literature reports (Coover and McIntire, 1989 and Schoenberg, 1985).

Table 3.  $\Delta H_p$  of the composites.

Formulation	$\Delta H_p$ (kJ/mol)
30T20H15P15M10Q	57.5
70T20H15P15M5Q	62.3
30T25H15P15M5Q	49.5
70T25H15P15M10Q	55.2
30T20H20P15M5Q	61.4
70T20H20P15M10Q	49.9
30T25H20P15M10Q	52.3
70T25H20P15M5Q	57.8
30T20H15P20M10Q	56.4
70T20H15P20M5Q	51.9
30T25H15P20M5Q	54.3
70T25H15P20M10Q	56.7
30T20H20P20M5Q	58.2
70T20H20P20M10Q	59.1
30T25H20P20M10Q	54.3
70T25H20P20M5Q	62.9
50T22H17P17M7Q	55.7

Perhaps, in a radical copolymerization, the hydroxyapatite act as capable agent to adsorb a part of heat (express as a polymerization or peak temperature,  $T_{max}$  in Fig. 2) generated by the process. It makes the interpretation of this phenomenon more complex what is presented in the reality, although in this cases the presence of HA as a load does not represent an influence over the polymeric matrix because the narrow range of the study (20-25) % (García, 2001).

It could be also attributed to the "mesophase" theory and the treatment of the filler surfaces, to achieve a better adhesion from the inorganic loads to the polymeric matrix (García, 2001 and Stupp and Ciegler, 1992). The superficial treatment with silane improves the adherence from filler particles to organic matrixes because the SiOH groups allows a better connection with the filler inorganic structure from the Si and connection type hydrogen bridge with polymeric molecules achieving a better absorption and an improvement of the composite properties (Veranes *et al.*, 2002).

#### B. Absorption and solubility studies.

The Fig. 5 shows the absorption values for all the sam-

ples. Similar to case of the working and setting times, these two properties are much related. For these reason, the behavior of absorption and solubility were very similar.

As seen in Fig. 5 (where 3T, 5T and 7T represents 30, 50 and 70 % of TEGDMA and 0H, 2H and 5H indicate 20, 22.5 and 25 % of HA) none of the samples performs the requirements recommended in the ISO regulation comparing with a norm whose application is in dental materials, where the values of absorption and solubility need to be below 40  $\mu\text{g}/\text{mm}^3$  and 7.5  $\mu\text{g}/\text{mm}^3$  respectively (ISO 2000).

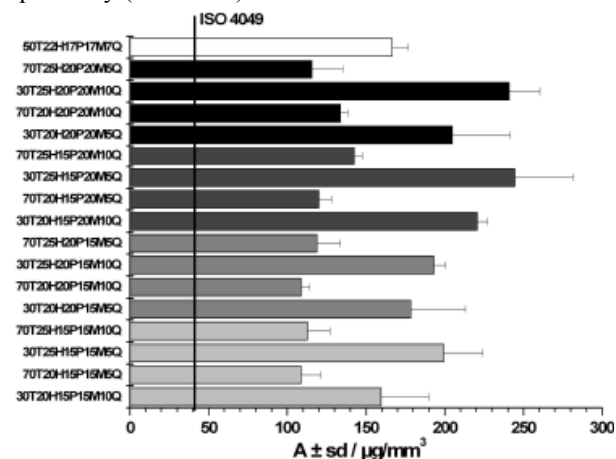


Figure 5. Absorption values of the samples.

In our case, where the possible application is in bone restorations or orthopedic surgery, some solubility (or absorption) of the sample is something interesting and desirable, because once the process occurs the weary composite surface made possible the contact between bone and hydroxyapatite filler. These facts make the composite more biocompatible and give more possibilities of success to implants, although the primary approach would be to maintain the values of absorption and solubility the lowest possible (Veranes *et al.*, 2006).

However, through the Fig. 5, we can consider the monomeric composition the most important variable because the highest differences between the absorption values are related with the variation in the monomeric composition. When the TEGDMA percent increases, the HEMA content decrease, which give to composite less capacity to establish a hydrogen bridge through OH group from HEMA and prevail the rigidity and hydrophobicity of TEGDMA (Patel and Braden, 1989).

$$A = 163 - 43A - 8B + 15D \quad (5)$$

$$S = 45 - 20A + 10B \quad (6)$$

Anywhere, the statistical treatment for both properties, as said before, presents the same tendency. Eqs. 5 and 6 show a strong dependency of monomeric composition for both properties, according with Fig. 5. Starting from the double interactions is not interesting for the statistical analysis; in the absorption (first process of both) influence more variables than the solubility, including the mentioned double interactions.

### C. Mechanical studies.

The compression strength of the composites involved in the studies is shown at the Fig. 6. The compression strength decreases with the addition of DMpT and BPO. If the polymerization reaction occurs very rapidly (highest values of amine and initiator, see discussion 3.A related with setting times) the polymeric network does not have the possibility to arrange the interconnection between polymeric matrix and hydroxyapatite filler. In our case, where the filler is not treated, the time for the better accommodation into a polymeric matrix is very important (García, 2001).

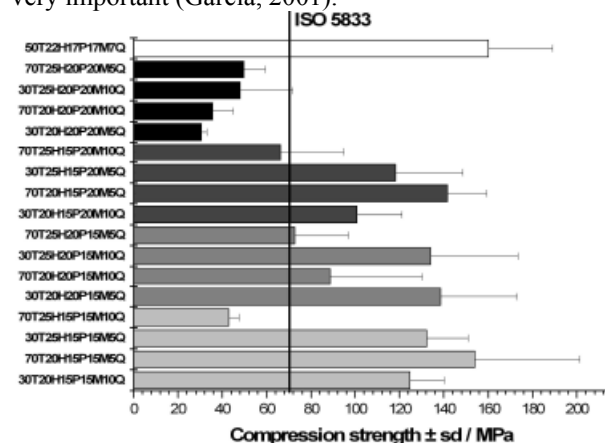


Figure 6. Compression strength of composites.

Anyway, the maximum values of compression strength ( $\approx 160$  MPa) are lowest than the values reported to dental materials (200 MPa) (ISO, 2000) and highest than reported for the acrylic bone cements (80-110 MPa) (Planell *et al.*, 1995). The differences with acrylic bone cements are comprehensible because the filler of these cements is the polymer (*i.e.* Palacos<sup>®</sup>, Subiton<sup>®</sup>, CMW<sup>®</sup>, Rostal<sup>®</sup>). It was also higher than the norms requirement to use as acrylic bone cement ( $> 70$  MPa) (ISO, 2002). Obviously, hydroxyapatite confers better compression strength to a polymeric matrix than a polymer himself (Morejón *et al.*, 2005). On other hand, comparing with dental materials, even when the composites samples use the same mechanism as dental obturants (two pastes system), the hydroxyapatite used as filler had a particle aggregate size below 160  $\mu\text{m}$  and it was non-treated. The more useful dentals obturants in the international market employees' hybrid materials with silanized quartz and calcium phosphates with a particle size 10-30  $\mu\text{m}$  and even smallest. That is to say, a hydroxyapatite with small size of particle and surface treatment should be composites a better adhesion inorganic filler-polymeric matrix, and then, better mechanical properties (García, 2001).

In case of elastic modulus, the behavior was similar. Only that in this case, the most important variables were the monomeric composition and amine percent. The tendency respect to amine percent was the same that in case of compression strength, which it expected. When the amine percent increase the polymerization process occur very rapidly and does not exist a possibility of

accommodation of the filler into a polymeric matrix (Moursi *et al.*, 2002 and Veranes *et al.*, 2002).

The Fig. 7 shows the tendency of elastic modulus vs. monomeric composition and amine percent. The case of monomeric composition was very clearly because when increase the TEGDMA content, it increase the rigidity of the composite too, the polymeric network is very hard and interconnected. Noted at highest values of TEGDMA percent, the differences between the values of elastic modulus are less than when it works at low TEGDMA percent, when the HEMA content, and in consequence the hydrophilic character of the sample, is higher (Ambrosio *et al.*, 1998).

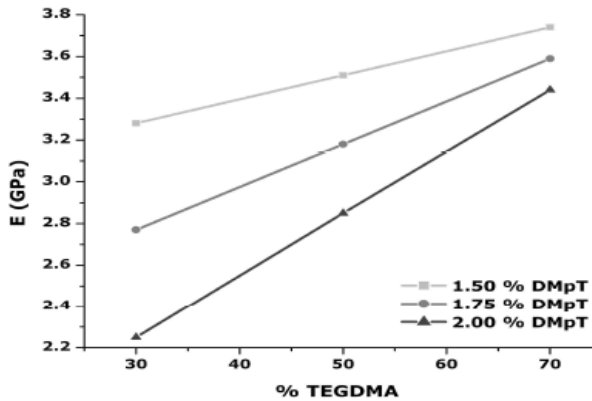


Figure 7. Tendency of elastic modulus vs. monomeric composition and amine percent.

The statistical treatment confirms significant influence of the amine percent in the mechanical properties and the importance of monomeric composition and initiator content. To improve the compression strength of the composites it must work with lower values of amine and initiator percent. On the contrary, better elastic modulus, must work with a higher content of hydrophobic monomer (T) and a higher value of amine.

**D. Drug release.**

From the analysis of the release profiles, only the samples 1, 3 and 11 in order to better look for the differences between each sample are shown at Fig. 8, reached the classic release profile as many other drug delivery systems (Fuentes *et al.*, 2005). Three cases (Table 2), are experiments where TEGDMA percent is the lowest, in other words, there is highest HEMA percent. The hydrophilic character of HEMA guarantees the highest values of release of these samples, where it supposed the monomeric composition is also the most important variable.

But coincidentally the amine percent is the second most important effect. The main difference in three cases should be other variables. For example, sample 11 has higher amine percent than sample 1 and 3. From these two samples, 1 has lower load than sample 3. Anyway, considering composites samples as non-porous releases matrices (Baker and Lonsdale, 1974) due to strongest hydrophobic character and from the Fig. 8, it is easy to think that the behavior of the composites release profiles is very complex.

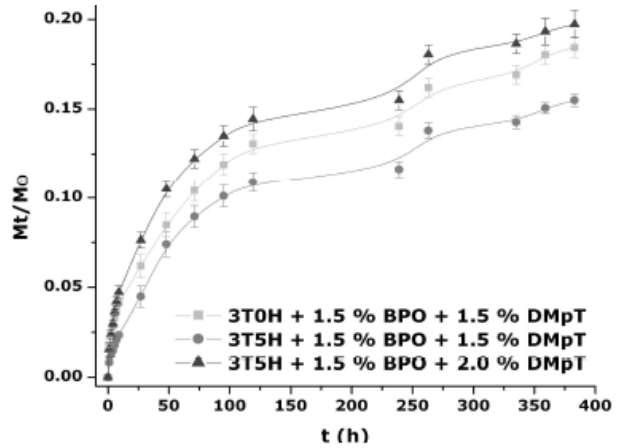


Figure 8. Release profile of the three best samples.

Higuchi (1961) considered drug release in some hydrophilic devices like a process dependent of diffusion. This process from any of the different forms of drug-polymer composites must be predictable and often a constant release rate (zero order) is desired (Higuchi, 1967). For many years a considerable amount of mathematical analysis of the theoretical rates of diffusional release from various fixed geometrical configurations has been reported and correlated with experimental results (Flynn *et al.*, 1974).

From previous works (Baker and Lonsdale, 1974 and Fuentes *et al.*, 2005), the Baker's treatment to the samples was applied (Fig. 9). In this case we analyze only the same three samples. The correlation between the variables was very good, all above 0.978 ( $r_{crit}(0.99,15) = 0.725$ ). The model coefficients had a statistical significant >99 %. From the first term of equation we calculated de diffusion coefficient (D), a parameter that shows the diffusion capacity of the samples (Patel and Braden, 1991). The second term is related with migration and dissolution of drug and justifies a double mechanism which shows a low concentration of drug in phosphate buffer at 15 days.

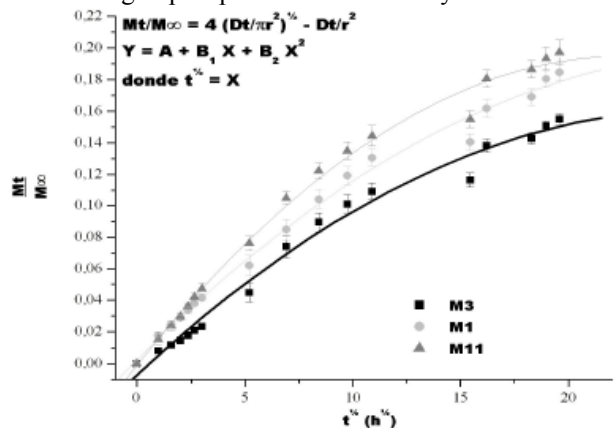


Figure 9. Baker's treatment applied to composites samples.

In case of calculus of diffusion coefficients the results guide, due to the little values and errors of determinations, that our matrixes does not diffuse so much (Fig. 10). Usually, the acrylic hydrogels have diffusion

coefficients in a range  $10^{-7}$  cm<sup>2</sup>/s, three orders bigger than composites samples. Of course, a filler like hydroxyapatite, very lightly soluble in water and fluids lead to this result. The use of hydrophobic monomers contributes to diminish this little value of diffusion (Hastings and Ducheyne, 1984).

In Fig. 11 we can observe the tendency of drug release percent vs. composition and amine. As we can see, when composition and amine content increase, the drug release percent diminishes. The explanation coincides with the discussion related to absorption and solubility and mechanical properties (Patel and Braden, 1991).

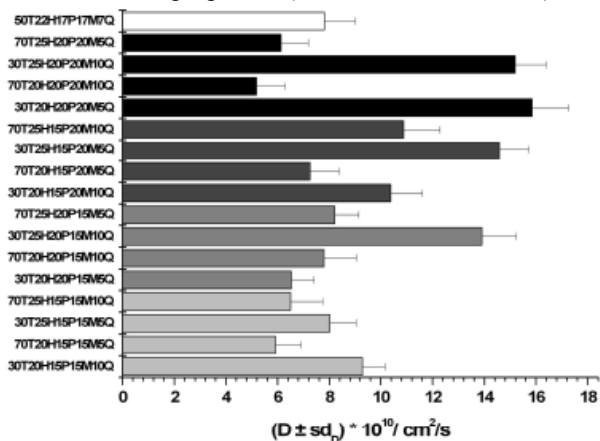


Figure 10. Diffusion coefficients of composites.

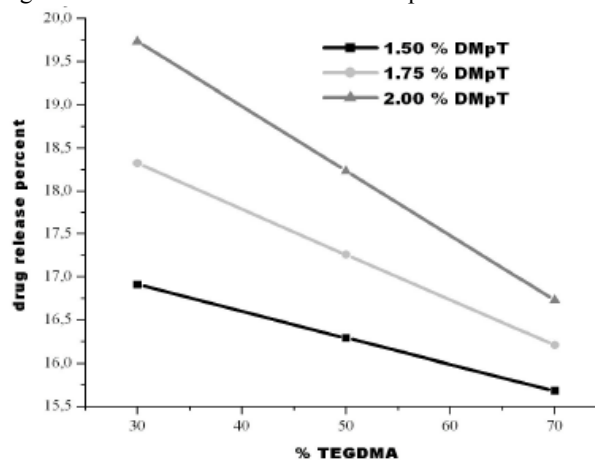


Figure 11. Tendency of drug release percent vs. composition and amine content.

#### IV. CONCLUSIONS

An experimental design to study the influence of the composition in several properties of composites loaded with hydroxyapatite was made. The results were according to expected and reproduced the results previously reported about composition influence over properties of composites but also provided new information related to the capacity of drug release from hydrophobic copolymers and a comparing the range approved by the international norms.

The working and setting time showed a strong dependency of amine and initiator content, three and two times more influential than composition and load. The time ranges were according to the international reports

for dental obturants and acrylic cements for orthopedics. The polymerization enthalpy was between ranges reported for the acrylic materials.

The absorption and solubility were lower than reported by previous works. The hydrophilic character provided by HEMA gave to composites values of absorption (six times) and solubility (seven times as average) higher than international norms for dentals materials. In case of mechanical properties, in some samples, we obtain better values than reported for the acrylic cements, although always lower than reported for the dental materials.

The drug release had a complex behavior cause a matrix had a range between hydrophobic and hydrophilic character and in function of that, the drug release percent oscillated in a range 15 -20 % in 15 days, very low, which support the theory of the composition importance over the composites properties.

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