

SUPERCRITICAL IMPREGNATION ISOTHERM OF O-HBA ON PMMA IN BATCH STIRRED REACTOR

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The aim of the present work is to quantify the amount of o-hydroxybenzoic acid (o-HBA) impregnated in poly(methyl metacrylate) (PMMA) in presence of supercritical carbon dioxide (SC CO₂) for a given temperature and pressure. A batch stirred reactor, equipped with sampling device, was used for that purpose. SC CO₂ is used as solvent and swelling agent, the swelling of the amorphous glassy polymer being favorable to the impregnation process. Two series of experiments were made. First, various quantities of pure o-HBA were entirely solubilized in the reactor in order to measure the concentration in the CO₂ phase. Concentrations were measured by regular sampling and posterior HPLC analysis. Secondly, same quantities of o-HBA were put together with 1g of PMMA. The impregnation of o-HBA in the polymer resulted in lower concentrations in the reactor. As the impregnation proceeds, the concentration decreases until it reaches a constant value when equilibrium is attained. The quantity of o-HBA impregnated by g of polymer was determined based on the difference between the concentrations measured for the sets of two experiments.

INTRODUCTION

The scientific and industrial interest for processes carried out in supercritical media is due to capability of SC fluids to replace some traditional toxic solvents, and to vary continuously solvent properties from gas to liquid [1]. SC carbon dioxide, used in this study as solvent and swelling agent, shows several advantages as non toxicity, relatively mild SC conditions allowing treatment of thermolabile substances, and small molecular size resulting in good penetrability. The high dissolving power, low viscosity and high diffusivity make SC fluids an ideal media for clean technology of impregnation of polymers with different additive molecules [2]. The high product purity (free of residual solvent) is important when concerning foods and pharmaceuticals. Synthesis of controlled-release products in SC medium allows for avoiding or reducing the utilization of organic solvent, and so to reduce costs for the removal of this solvent [3]. Processing PMMA-based polymers with SC-CO₂ leads to polymer swelling (and plasticization), which facilitates the active agent infusion into polymeric phase [4]. The final removal of the SC-solvent is easily performed by simple depressurization. The solute is o-hydroxybenzoic acid, because of its higher solubility compared to m- and p-hydroxybenzoic acid [5]. The polymer and the active substance were chosen as model compounds for

pharmaceutical application, with an aim of collecting experimental data for modeling of the impregnation in SC medium.

1- MATERIALS AND EQUIPMENT

Materials

The polymer PMMA is received from Departamento de Química Macromolecular, Instituto de Ciencia y Tecnología de Polímeros, CSIC, Juan de la Cierva 3, 28006 Madrid, Spain. The powder consists in spherical PMMA beads of diameter 125-250 μm .

Hydroxybenzoic acid (o-HBA; NORMAPUR' purity 99.8%) is purchased from Prolabo.

Methanol (HPLC-grade purity) is purchased from Prolabo.

1M acetic acid solution was prepared with glacial acetic acid.

CO₂ is supplied from Messer.

Equipment

A schematic flow-sheet of the equipment is given in Figure 1.

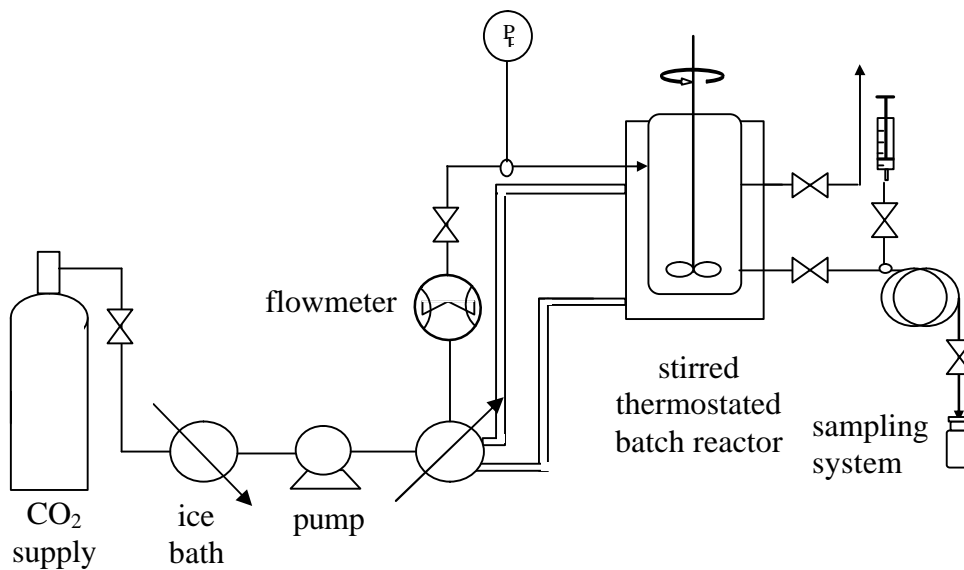


Figure 1. Experimental equipment

The compression module consists in a CO₂ cylinder, a chiller (2°C) and a piston pump LEWA EKM-10. The liquefied CO₂ is supplied by the pump to the reactor after heating. The operational pressure is 12MPa and the operational temperature is 40°C.

The batch reactor is thermostated by a water recirculation and a constant temperature water bath. The stirring rate was settled at 650 rpm. The internal reactor diameter and height are 40mm and 80mm respectively, giving an internal volume of 100ml. The distance from the

reactor bottom to the impeller is 5mm . PMMA and/or series of different quantities of o-HBA are introduced in the reactor. The CO_2 is further introduced and the stirring is activated.

Samples are taken regularly via a sampling system of 1ml . The content of the sampling device is collected by rinsing with methanol. The sample is analysed by liquid chromatography (HPLC) system, previously calibrated for detection of o-HBA. The mobile phase consists in a mixture of methanol and 1M acetic acid solution, in proportion of 60:40. The mobile phase flow rate is $1\text{ml}/\text{min}$. The wavelength is $\lambda=300\text{nm}$. The peak area is converted to concentration via calibration curve with linear regression $R^2=0.997$.

2. METHOD

The method presented hereby is developed to measure the amount of active substance adsorbed in a polymer matrix in supercritical medium. Temperature and pressure are constants. The data obtained are presented as isotherm curves, i.e. the quantity of substance impregnated per g of polymer as a function of the concentration of solute in the supercritical solvent. Data obtained will be further incorporated into a mass-transfer model describing a semi-continuous impregnation process.

In order to get the $Q=f(C)$ curves, 2 sets of experiments were performed:

1 set: The first task was to do a serie of experiments without polymer. Different quantities of o-HBA were entirely solubilized in the reactor and corresponding concentrations were determined by sampling and HPLC. 60mg was the maximal amount that can be solubilized in the reactor.

2 set: Same known quantities of o-HBA were put in the reactor with 1g of PMMA. The impregnation of o-HBA in the polymer give lower concentrations in the reactor detected by regular sampling and posterior HPLC treatment. Due to the stirring of the reactor, the concentration quickly tends to a constant value. The difference between the concentrations detected during every set of experiments (with and without polymer) allowed for calculation of the quantity of o-HBA impregnated. Presenting this value as $\text{mg o-HBA}/\text{g PMMA}$ and plotting versus concentration in $\text{mg o-HBA}/\text{g CO}_2$, we obtained the impregnation isotherm for the operational temperature-pressure couple.

Three experiments were made at $P=16\text{MPa}$ and $T=40^\circ\text{C}$ to assess the reproducibility of the method. The error over the amount of substance impregnated in the PMMA is within $\pm 2\%$.

3. RESULTS AND DISCUSSION

Quantities of o-HBA from 4mg to 60mg were used. First, an experiment is carried out with each amount of HBA, and the concentration in the fluid phase is plotted versus time. The solubilisation process in the stirred batch reactor is quick and the concentration after 10min tends to a constant value (open marks in **figure 2**). Then, the concentrations obtained at the plateau are plotted versus respective quantities and fitted with linear regression ($R^2=0,98$). These data are considered as reference concentration and are correlated to the mass of solute put in the reactor. For 60mg o-HBA, we were close to the saturation value at the operational couple temperature-pressure. The corresponding concentration ($P=12\text{MPa}$ and $T=40^\circ\text{C}$) was

$y=1,986*10^{-4} \text{ mol } o\text{-HBA/molCO}_2$. That saturation value is in the same order of magnitude than those reported by other authors [5,6], as shown in the next table (**table1**).

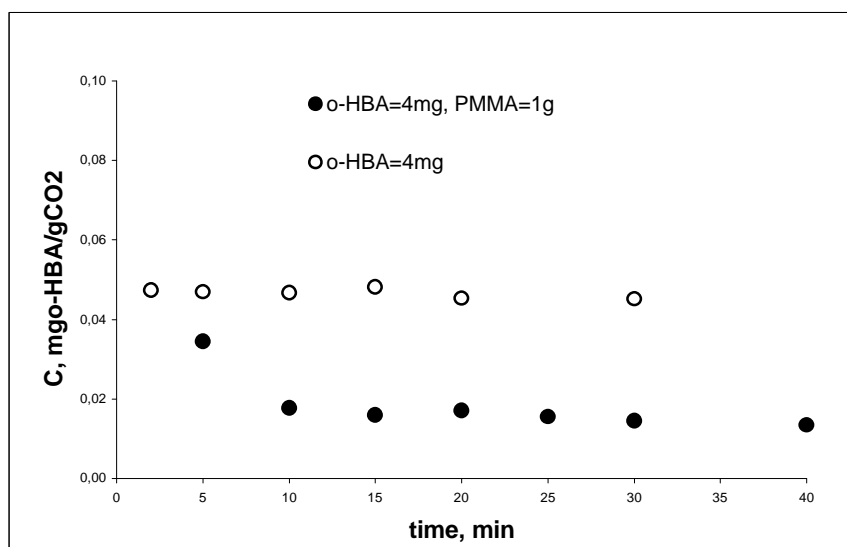


Figure 2. Variation of the concentration plotted versus time (o-HBA=4mg)
 open symbol: without polymer – no impregnation
 dark symbol: with polymer – impregnation effect

| P (bar) | Solubilité , $y \times 10^4$ [6] |
|---------|----------------------------------|
| 111.4 | 1.63 |
| 121.6 | 1.92 |
| 131.7 | 2.23 |
| P (bar) | Solubilité , $y \times 10^4$ [7] |
| 100 | 1.05 |
| 115 | 1.94 |
| 130 | 2.80 |

Table 1. Solubility o-HBA in SC-CO₂ [mol/mol] reported by authors [5,6].

The second set of experiments is made with known amount of o-HBA and 1g PMMA in the reactor. As shown by dark symbols in **figure 2**, the concentration of the solute is decreasing rapidly. The difference between the curves obtained with and without polymer is due to the impregnation, i.e. the partition of o-HBA between the SC phase and the polymer phase. The impregnated amount is then easily calculated from the value at the plateau. The impregnated quantity, (expressed in *mg* o-HBA/gPMMA) plot as a function of concentration (expressed in *mg* o-HBA/g CO₂) represents the impregnation isotherm for the operational temperature-pressure couple.

The isotherm at 12MPa and 40°C is given in **Figure 3**.

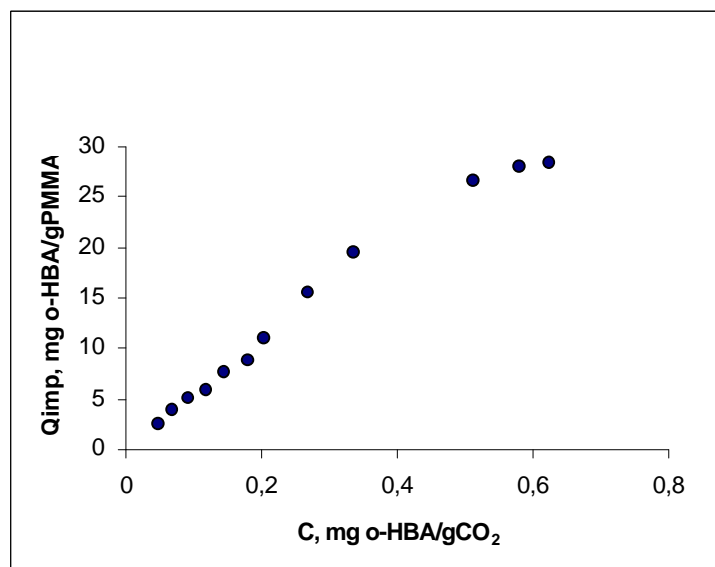


Figure 3. Impregnation isotherm of HBA on PMMA : $P=12MPa$, $T=40^{\circ}C$

The quantity taken by the polymer is increasing as the concentration in the fluid phase increases. At concentrations above $0.6mg/gCO_2$, the isotherm seems to reach a plateau. As mentioned before, it was not possible to work with higher concentrations, because it exceeded the saturation value. The shape of the curve may suggest an isotherm of type II or IV [7], that are characteristic for multilayer adsorption and possible capillary condensation. Examples of impregnation and specially isotherm determination for polymers are scarce in literature. But hypothesis of multilayer adsorption, due to the swelling of polymer, does not seem unrealistic.

CONCLUSIONS

Isotherms of impregnation of PMMA with o-HBA have been determined experimentally in a stirred reactor, with regular sampling and chromatography analysis. The saturation value of PMMA with o-HBA was found to be within $25mg/g$, at $12MPa$ and $40^{\circ}C$. Extra experiments are currently carried out to obtain isotherms for various pressures up to $20MPa$. The obtained $Q=f(C)$ relation will be further introduced in a model, whose aim is to describe a semi-continuous impregnation process of a fixed bed of polymer.

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