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# Preparation of Microparticles of Polycaprolactone Containing Piroxicam to use in Chronic Inflammatory Diseases

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**Abstract** The microparticles containing piroxicam were produced by the oil-in-water emulsion-solvent evaporation technique, and characterized by microscopy, loading efficiency, size distribution and polydispersity index, *in vitro* drug release and release kinetics. A total of 20 formulations were prepared and characterized. Microparticles presented micrometric size of 1.026µm to 3.541µm, distribution homogeneous with PDI below 0.35 with spherical and regular shape. The piroxicam loading efficiency varied from 47.9 to 91.0% (w/w). In the release study, between 10.66 to 36.36% of piroxicam was released to the dissolution medium after 6 hours. The most appropriate formulation was F3 containing 10mg of the drug because of the high encapsulation efficiency, high encapsulated drug content and sustained release. The results demonstrated that it is possible to obtain microparticles with good morphological and release characteristics using the method oil-in-water emulsion-solvent evaporation.

**Keywords** chronic inflammation, microparticles, piroxicam, prolonged release.

## Introduction

The microparticles are Controlled Drug Delivery Systems that offer the advantage of maintaining the concentration of the drug in the therapeutic range after a single dose avoiding fluctuations in the plasma concentration [1]. The microparticles have greater chemical and physical storage stability, increase the bioavailability of the drug, decrease local and systemic side effects, and provide the encapsulation of lipophilic and hydrophilic drugs to be encapsulation [2]. Physical and chemical processes as water penetration into the matrix or diffusion of the drug through matrix pores by degradation of the polymer are involved in the release [3].

The development of the microparticles is based on the association of the drugs with polymeric materials. The polymers may be natural (gelatin, gum arabic, chitosan) or synthetic biodegradable polymers (lactic acid, glycolic acid, polycaprolactone) [4]. The choice of the encapsulating material depends of the physical and chemical characteristics of the drug, the intended use, and the technique used to form the microparticles [5].

The polycaprolactone (PCL) is a synthetic polymer, biodegradable and biocompatible of the aliphatic polyester class. The good solubility and biocompatibility allows applications in the pharmaceutical industry because of the ability to be reabsorbed by the body [6]. The PCL undergoes degradation by the hydrolysis of the ester linkages, generating ε-hydroxycaproic acid. However, because of the high hydrophobicity, this reaction is slow and does not produce an acidic environment as occurs with other polymers like PLA and PLGA. This is an advantage of PCL in the development of microparticles containing proteins, because these macromolecules can denature in acid pH and lose their activity [7].

The oil-in-water emulsion-solvent evaporation method is most used to prepare microparticles due to the simplicity and the possibility of obtaining microparticles with defined characteristics. This method is based on the formation of

an emulsion oil-in-water (o/w). The drug is dissolved in the organic phase containing the polymer. After, there is an emulsification of the organic phase in an aqueous phase containing a surfactant to prevent aggregation and coalescence. The solvent is removed by application of vacuum or evaporation at room temperature to production a suspension of drug-loaded in polymeric microparticles that can be separated by centrifugation [2].

The encapsulation of some drugs can be advantageous. Anti-inflammatory drugs, such as Piroxicam (PXC), may have a prolonged time of action by microencapsulation, also decreasing adverse effects [8].

The 4-hydroxy-2-methyl-1,1-dioxo-N-pyridin-2-yl-1,2-benzothiazine-3-carboxamide, or Piroxicam, is a nonsteroidal oxicam derivative with anti-inflammatory, antipyretic and analgesic properties, and acts by inhibiting the cyclooxygenase-1 and cyclooxygenase-2 enzymes in a non-selective manner [9]. The effects of anti-inflammatories result from the inhibition of both isoforms of cyclooxygenases which convert arachidonic acid to prostaglandins. Thus, there is a reduction in the synthesis of prostaglandins, decreasing the inflammatory process [10]. The Piroxicam has many adverse effects like nausea, diarrhoea, bleeds or ulceration of the stomach, constipation, abdominal pain, and dizziness. The chronic use of this anti-inflammatory may enhance adverse effects such as irritation of the gastric mucosa. Thus, the development of an extended release system may reduce the frequency of administration and render treatment more effective with less adverse effects. The treatment of arthritis and arthrosis could be done by the intra-articular administration of piroxicam encapsulated in the microparticles [10].

The present work had as objectives to obtain microparticles of polycaprolactone containing Piroxicam by the oil-in-water emulsion-solvent evaporation technique, standardization of the methodology for drug quantification by spectrophotometry, determination of loading efficiency, characterization by optical microscopy and size distribution and polydispersity index, *in vitro* drug release, and study of the release kinetics by the application of the mathematical models Order Zero, First Order and Higuchi.

## Materials and Methods

### Materials

Acetone, methanol and dichloromethanewere purchased from Merck. Piroxicam, polyvinyl alcohol polycaprolactone (average Mw ~14,000 and average Mw45,000) were purchased from Sigma-Aldrich.

### Methods

### Preparation of Microparticles

The microparticles were prepared by the oil-in-water emulsion-solvent evaporation technique (Figure 1). The polymer (polycaprolactone) and the drug (Piroxicam) were dissolved in organic solvent (dichloromethane) and then emulsified in an aqueous phase containing surfactant (polyvinyl alcohol), under stirring, using the UltraTurrax apparatus, for five minutes.

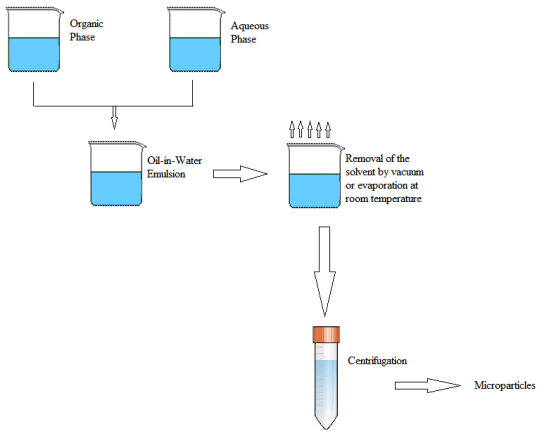


*Figure 1: Emulsion and solvent evaporation method*

The conditions of preparation of the microparticles such as homogenization rate, polymer mass, drug mass, type of polymer and amount of organic solvent were modified to verify the influence of these parameters on the characteristics of the microparticles.

Two batches of Polycaprolactone were tested. One with molecular weight 45,000 and other with molecular weight 14,000. The table 1 shows the formulations prepared.

**Table 1**: Formulation of the microparticles

| Formulation | PCL (mg) | PRX (mg) | PVA (mg) | Dichloromethane (mL) | Ultra Turrax Speed (rpm) | MW of the polymer |
|---|---|---|---|---|---|---|
| *0 | 180 | 20 | 500 | 10 | 6,000 | 45,000 |
| 1 | 180 | 20 | 500 | 10 | 6,000 | 45,000 |
| 2 | 185 | 15 | 500 | 10 | 6,000 | 45,000 |
| 3** | 190 | 10 | 500 | 10 | 6,000 | 45,000 |
| 4 | 195 | 5 | 500 | 10 | 6,000 | 45,000 |
| 5 | 190 | 10 | 500 | 10 | 14,000 | 45,000 |
| 6 | 180 | 20 | 500 | 10 | 6,000 | 14,000 |
| 7 | 185 | 15 | 500 | 10 | 6,000 | 14,000 |
| 8** | 190 | 10 | 500 | 10 | 6,000 | 14,000 |
| 9 | 195 | 5 | 500 | 10 | 6,000 | 14,000 |
| 10 | 190 | 10 | 500 | 10 | 14,000 | 14,000 |
| 11 | 360 | 20 | 250 | 20 | 6,000 | 45,000 |
| 12 | 370 | 15 | 250 | 20 | 6,000 | 45,000 |
| 13*** | 380 | 10 | 250 | 20 | 6,000 | 45,000 |
| 14 | 390 | 5 | 250 | 20 | 6,000 | 45,000 |
| 15 | 360 | 20 | 250 | 20 | 6,000 | 14,000 |
| 16 | 370 | 15 | 250 | 20 | 6,000 | 14,000 |
| 17*** | 380 | 10 | 250 | 20 | 6,000 | 14,000 |
| 18 | 390 | 5 | 250 | 20 | 6,000 | 14,000 |
| 19 | 200 | - | 500 | 10 | 6,000 | 45,000 |

* F0: passive evaporation with magnetic stirring at ambient conditions

** Comparison between F3 and F8 (*in vitro* release studies)

*** Comparison between F13 and F7 (*in vitro* release studies)

PCL-polycaprolactone, PVA-polyvinyl alcohol, PRX- Piroxicam, MM –molecular weight of the polymer, EL-Loading Efficiency, PDI- polydispersity index, SD- Standard deviation

After emulsion was prepared, the rotavaporator was used to evaporate the solvent, leaving the emulsion for 1 hour in the apparatus. With the purpose of comparing the procedures and verifying if there is influence in the encapsulation process, a formulation (F0) was also prepared using passive evaporation with magnetic stirring at room temperature for 24 hours.

**Study of Microparticle Morphology by Optical Microscopy**

The microparticles were fixed in a slide. The analyzes for the observation of the shape, surface and size were performed by optical microscopy. The microscope used was binocular of the Quimis line. The increase was 40x and the images were viewed on a computer with the aid of a camera built into the microscope.

**Size Distribution and Polydispersity Index**

The size distribution and polydispersity index of the microstructured systems can be measured using the light scattering module of the ZetaSizer equipment (Malvern Instruments). The microparticles were diluted in purified water and analyzed for the mean diameter and polydispersity index. The analysis was done in triplicate.

**Loading Efficiency**

The loading efficiency was determined by a centrifugation method followed by quantification of the free drug by UV-Vis spectrophotometry [11-12].

L.E. = (total drug - free drug)/total drug x 100

The sample was divided into two Falcon tubes, which were placed in the centrifuge, with a shaking of 8000 rpm for 20 minutes. The microparticles were then separated from the supernatant, washed with distilled water and centrifuged once more. To determine the encapsulation efficiency, the solubility of the polymer and the drug in hot acetone was checked, because it is necessary to use a solvent that breaks the capsule and extracts the drug.

**Spectrophotometry**

A stock solution of Piroxicam in acetone was prepared in a 100mL volumetric flask to detect the wavelength of maximum drug absorbance. Then, from this solution, 10 concentrations of 0.7936µg/mL to 7.4074µg/mL were prepared for analysis in a spectrophotometerV-630 (Jasco). With the results found, an analytical curve was made using Excel software. To obtain the linearity criteria for acceptance of the curve, the correlation coefficients and the line equation were used. The minimum acceptable criterion of the correlation coefficient (r) should be 0.99. The microparticles obtained after centrifugation were dissolved in hot acetone, and the solution was analyzed in the spectrophotometer. The drug concentration was calculated from the line equation obtained through the calibration curve, and the loading efficiency was estimated using equation (L.E.).

***In vitro* Drug Release**

To determine the release profile, a thermostated bath with a controlled temperature of 37ºC was used. To the bath were added beakers containing phosphate buffer saline (pH = 7.4) (receiver medium), which constituted the recipient compartment. Under these compartments were placed the donor compartments containing dissolved microparticles in buffer solution. The system was kept under magnetic stirring, and the experiment was carried out in triplicate. A stock solution of Piroxicam in methanol was prepared in a 100mL volumetric flask. Then, from this solution, 10 concentrations of 0.7936 to 7.4074µg/mLin receiver medium of the release study were prepared for analysis in a spectrophotometer. With the results found, an analytical curve was made using Excel software. Aliquots were withdrawn from the bath at predetermined time intervals, and analyzed by ultraviolet absorption at the wavelength of maximum drug absorbance. After the analysis, the aliquot was transferred to the respective beaker for the continuation of the release test. The drug concentration was calculated from the line equation obtained through the calibration curve. From the obtained concentrations, a graph of the release profile was constructed.

**Release Kinetics**

Several theories and mathematical models describe the release kinetics of the drug from pharmaceutical form. The most widely applied release models that best describe the phenomenon of drug release are Higuchi, zero order, first order, Hixson–Crowell, Weibull, Baker–Lonsdale, Korsmeyer–Peppas and Hopfenberg models[13].

The zero order kinetics is applied to pharmaceutical forms that do not disaggregate and release the same amount of drug per unit time. It is an ideal method of drug release to achieve a prolonged pharmacological action, since the release is slow. This model can be represented by the equation $Qt = Q_0 + K_0t$, where Qt is the amount of drug dissolved in time t, $Q_0$ is the initial amount of the drug in the solution, and $K_0$ is the zero order release constant [13]. First order kinetics is characteristic of pharmaceutical forms whose release of the drug is proportional to the amount of drug remaining inside, so that the amount of drug released per unit time decreases over time. This model can be represented by the equation $\ln Qt = \ln Q_0 + Kt$, where Qt is the amount of drug dissolved in time t, $Q_0$ is the initial amount of the drug in the solution, and $K_0$ is the first order release constant [13]. Higuchi developed several theoretical models to study the release of water soluble and low soluble drugs incorporated in semi-solid and/or solid matrixes, and describes drug release as a diffusion process based in the Fick's law, square root time dependent. This model can be represented by the equation $Qt = KH + \sqrt{t}$, where Qt is the amount of drug dissolved in time t, and KH is the Higuchi dissolution constant [13]. The zero order, Higuchi and first order kinetics models were applied to the

release profiles presented in order to obtain the most suitable model for each profile performed. The choice of the best model was made from the linear correlation coefficient (r) obtained in each linear regression analysis.

## Results and Discussion

### Characterization of microparticles

Figure 2 shows optical microscopy of the microparticles. Figure 2A refers to the empty microparticles where we can observe that the particles are spherical. Figure 2B shows Piroxicam encapsulated in microparticles obtained by the process involving evaporation and passive solvent elimination at room temperature and magnetic stirring. The particles formed are spherical with a regular surface, but with the presence of crystals of the drug on the surface. Figures 2C to 2T show Piroxicam encapsulated in microparticles obtained by the process involving rotavaporator and active solvent elimination by vacuum. The particles formed are spherical, with a regular surface, and without the presence of crystals of the drug on the surface. Thus, active evaporation using vacuum was important for the microencapsulation process avoiding formation of the drug crystals.

From microscopy, it was observed that the sample remaining on the magnetic stirrer and evaporation at room temperature produced unencapsulated crystals of Piroxicam due to the slow removal of the solvent which caused the drug to escape into the aqueous phase and crystallization (Figure 2B). This was because a rapid elimination of the solvent in the rotavaporator is necessary to avoid the crystallization of the drug, allowing the complete encapsulation of Piroxicam in the polymer particles.The change of polymer did not significantly alter the morphology of the microparticles.

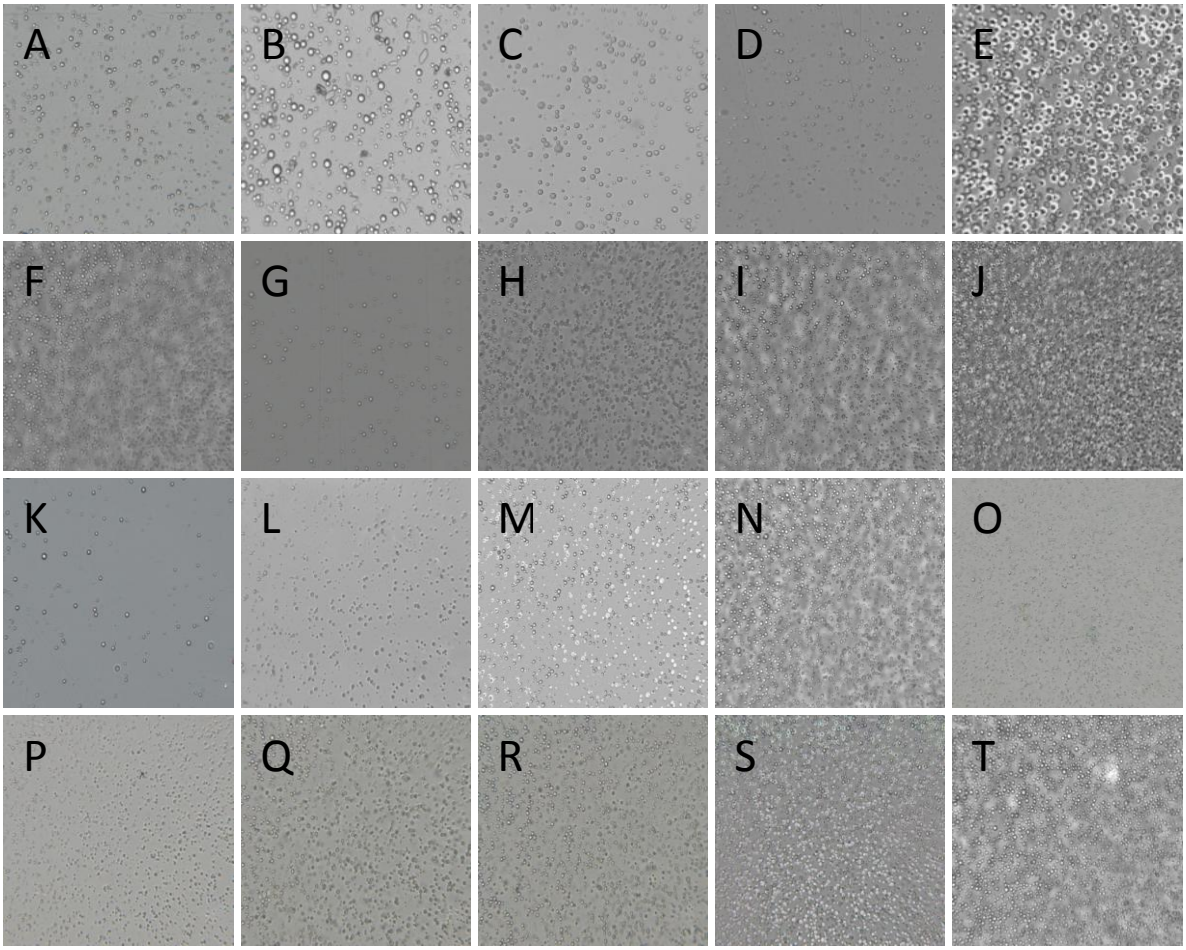


*Figure 2:* A) Microparticles without the drug (F19); B) Formulation with 20mg of the drug, prepared using the magnetic stirrer (F0); C) Formulation with 20mg of the drug prepared using high molecular weight polymer (F1);

D)Formulation with 20mg of the drug prepared using low molecular weight polymer (F6); E) Formulation with 20mg of the drug prepared using double the high molecular weight polymer (F11); F) Formulation with 20mg of the drug prepared using double the low molecular weight polymer (F15); G) Formulation with 15mg of the drug prepared using high molecular weight polymer (F2); H) Formulation with 15mg of the drug prepared using low molecular weight polymer (F7); I) Formulation with 15mg of the drug prepared using double the high molecular weight polymer (F12); J) Formulation with 15mg of the drug prepared using double the low molecular weight polymer (F16); K) Formulation with 10mg of the drug prepared using high molecular weight polymer (F3); L) Formulation with 10mg of the drug prepared using low molecular weight polymer (F8); M) Formulation with 10mg of the drug prepared using double the high molecular weight polymer (F13); N) Formulation with 10mg of the drug prepared using double the low molecular weight polymer (F17); O) Formulation with 10mg of the drug prepared using high molecular weight, in speed 14,000rpm (F5); P) Formulation with 10mg of the drug prepared using low molecular weight, in speed 14,000rpm (F10); Q) Formulation with 5mg of the drug prepared using high molecular weight (F4); R) Formulation with 5mg of the drug prepared using low molecular weight (F9); S) Formulation with 5mg of the drug prepared using double the high molecular weight polymer (F14); T) Formulation with 5mg of the drug prepared using double the low molecular weight polymer (F18).

**Size Distribution and Polydispersity Index**

The results of size distribution and polydispersity index are described in table 2. According to the characterization of the microparticles, performed in Zetasizer, it was observed that the particles obtained micrometric size with polydispersity index below 0.35 indicating a monomodal distribution. In Table 2, for the high molecular weight polymer formulations, we can observe an increase in particle size when the amount of polymer is increased and the amount of drug is decreased from 20mg to 5mg. For formulations containing the low molecular weight polymer, there was also an increase in particle size with decreasing amount of drug. However, when the concentration of Polycaprolactoneis folded, only the formulations F15 and F16 have become larger, unlike the formulations F17 and F18 that have the least amount of drug to be encapsulated. With increasing homogenization speed, there was a decrease in the size of the microparticles, as expected. By varying the rate of homogenization in Turrax® for emulsion preparation, the size of the microparticles decreases because the size is primarily influenced by the speed of agitation.

**Loading Efficiency**

A peak of maximum absorbance of Piroxicam was observed at 354nm. The analytical curve was linear in the concentration range of 0.7936 to 7.4074μg/mL in acetone, with a correlation coefficient above 0.99.

The results of Loading Efficiency are described in Table 2. According to the amount of drug used, the loading efficiency decreases when the mass of Piroxicam is increased from 5mg to 20mg. The same occurred when using the low molecular weight polymer. The decrease in Efficiency may occur due to the limited encapsulation ability of the polymer, leading to an exit of the drug into the aqueous phase. The drug is poorly soluble in water, but presents some solubility in this medium. By varying the rate of preparation, a lower encapsulation efficiency was obtained. It is concluded that by disrupting the system, there is a tendency for Piroxicam to move from the particles formed by the polymer to the external aqueous phase. When the amount of the polymer was doubled two different situations occurred in relation to Load Efficiency. When we compared the Efficiency of the formulations F1 and F2 with the formulations F11 and F12 there was an increase of Loading Efficiency with the increase of the amount of encapsulating polymer. However, when we compared the Loading Efficiency of the formulations F3 and F4 with the formulations F13 and F14 a decrease of Efficiency occurred with the increase of the amount of encapsulating polymer. It was observed that by doubling the amount of polymer, the Loading Efficiency for all formulations remained at 60%.

The same situation was observed for the formulations obtained with lower molecular weight polymer. When we compared the Efficiency of the formulations F6 and F7 with the formulations F15 and F16 there was an increase of Loading Efficiency with the increase of the amount of encapsulating polymer. However, when we compared the

Loading Efficiency of the formulations F8 and F9 with the formulations F17 and F18 a decrease of Efficiency occurred with the increase of the amount of encapsulating polymer. It was observed that by doubling the amount of polymer, the Loading Efficiency for all formulations remained at 65%.

**Table 2**: Results of Loading Efficiency, PDI and Size

| F | PCL (mg) | PRX (mg) | Ultra Turrax Speed (rpm) | MM of the polymer | EL* (%) | Drug* Content (mg) | PDI ± SD* | Size (μm) ± SD* |
|---|---|---|---|---|---|---|---|---|
| 1 | 180 | 20 | 6,000 | 45,000 | 48.8±0.53 | 9.8±0.11 | 0.231 ±0.019 | 1.462 ±0.022 |
| 2 | 185 | 15 | 6,000 | 45,000 | 52.3±0.42 | 7.8±0.10 | 0.258 ±0.033 | 1.935 ±0.608 |
| 3 | 190 | 10 | 6,000 | 45,000 | 84.5±0.19 | 8.5±0.02 | 0.278 ±0.043 | 1.970 ±0.142 |
| 4 | 195 | 5 | 6,000 | 45,000 | 80.0±0.35 | 4.0±0.02 | 0.154 ±0.118 | 1.948 ±0.513 |
| 5 | 190 | 10 | 14,000 | 45,000 | 55.9±0.23 | 5.6±0.02 | 0.165 ±0.048 | 1.135 ±0.242 |
| 6 | 180 | 20 | 6,000 | 14,000 | 49.6±0.56 | 9.9±0.11 | 0.263 ±0.061 | 1.900 ±0.615 |
| 7 | 185 | 15 | 6,000 | 14,000 | 47.9±0.78 | 7.2±0.12 | 0.137 ±0.076 | 1.026 ±0.027 |
| 8 | 190 | 10 | 6,000 | 14,000 | 91.0±0.45 | 9.1±0.05 | 0.158 ±0.095 | 2.802 ±0.056 |
| 9 | 195 | 5 | 6,000 | 14,000 | 79.1±0.55 | 3.9±0.03 | 0.334 ±0.051 | 2.541 ±0.514 |
| 10 | 190 | 10 | 14,000 | 14,000 | 59.0±0.43 | 5.9±0.04 | 0.271 ±0.124 | 0.658 ±0.052 |
| 11 | 360 | 20 | 6,000 | 45,000 | 62.4±0.56 | 12.5±0.11 | 0.170 ±0.058 | 2.080 ±0.957 |
| 12 | 370 | 15 | 6,000 | 45,000 | 60.9±0.78 | 9.1±0.12 | 0.169 ±0.125 | 2.308 ±1.266 |
| 13 | 380 | 10 | 6,000 | 45,000 | 67.5±0.65 | 6.8±0.07 | 0.148 ±0.077 | 2.412 ±1.161 |
| 14 | 390 | 5 | 6,000 | 45,000 | 62.9±0.87 | 3.2±0.06 | 0.131 ±0.206 | 2.728 ±1.232 |
| 15 | 360 | 20 | 6,000 | 14,000 | 66.5±0.54 | 13.3±0.11 | 0.109 ±0.080 | 2.268 ±0.832 |
| 16 | 370 | 15 | 6,000 | 14,000 | 58.8±0.36 | 8.8±0.05 | 0.234 ±0.082 | 2.812 ±0.460 |
| 17 | 380 | 10 | 6,000 | 14,000 | 65.6±0.78 | 6.6±0.08 | 0.170 ±0.124 | 1.488 ±0.235 |
| 18 | 390 | 5 | 6,000 | 14,000 | 67.5±0.47 | 3.4±0.02 | 0.294 ±0.060 | 1.287 ±0.263 |

PCL-polycaprolactone, PRX- Piroxicam, MM –molecular massofthepolymer, EL- LoadingEfficiency, PDI-polydispersity index, SD- Standard deviation

*Results are expressed as mean and standard deviation of n = 3 determinations

***In vitro* Drug Release**

A peak of maximum absorbance of Piroxicam was observed at 355nm. The analytical curve was linear in the concentration range of 0.7936 to 7.4074μg/mL in receptor medium of the release study, with a correlation coefficient above 0.99.

The release assays were performed for the formulations 1,2,3,4,8,13 and 17. The determination of the release rate of Piroxicam was evaluated after determination of drug concentration in the dissolution medium. All formulations were able to prolong the release of the drug. However, the release can be affect by microparticle size and drug distribution within thepolymeric matrix. A faster release can be relatedto the presenceof drug crystals on the microparticle surfaces. The location of the drug inside of the particles decreases release, and it is a result of the faster extraction of the organic solvent from the internal phase of the emulsion. From the release tests, when comparing formulations F1, F2, F3 and F4 (Figure 3a), there was a greater release of Piroxicam in F1 due to the fact that it had a larger amount of the encapsulated drug (20 mg) (Table 1). Lower release was observed in F4 due to the high encapsulation efficiency and the low amount of drug in the polymeric matrix (5 mg) (Table 1). The resistance of the polymer to the release is greater in delivery system with low amount of drug in the polymeric matrix (Formulation F4).

No major change in the drug release profile was observed by changing the higher molecular weight polymer to one of lower weight (Figure 3b and 3c).When comparing the release profile of formulations F3 and F8 (Figure 3b) with F13 and F17 (Figure 3c) we observed that the increase in the amount of polymer (See Table 1) reflected in a higher

release rate. One of the explanations for this increase in release rate may have been in the form of distribution of the drug molecules in the polymeric structure of the microparticles. Thus, increasing the amount of polymer may have displaced the drug into the more superficial layers of the microparticles with an increase in release rate. Than, it is concluded that the encapsulation of Piroxicam in microparticles succeeded in prolonging the release of the drug. It can be seen that during the test hours, no release of the entire drug from the particles occurred.

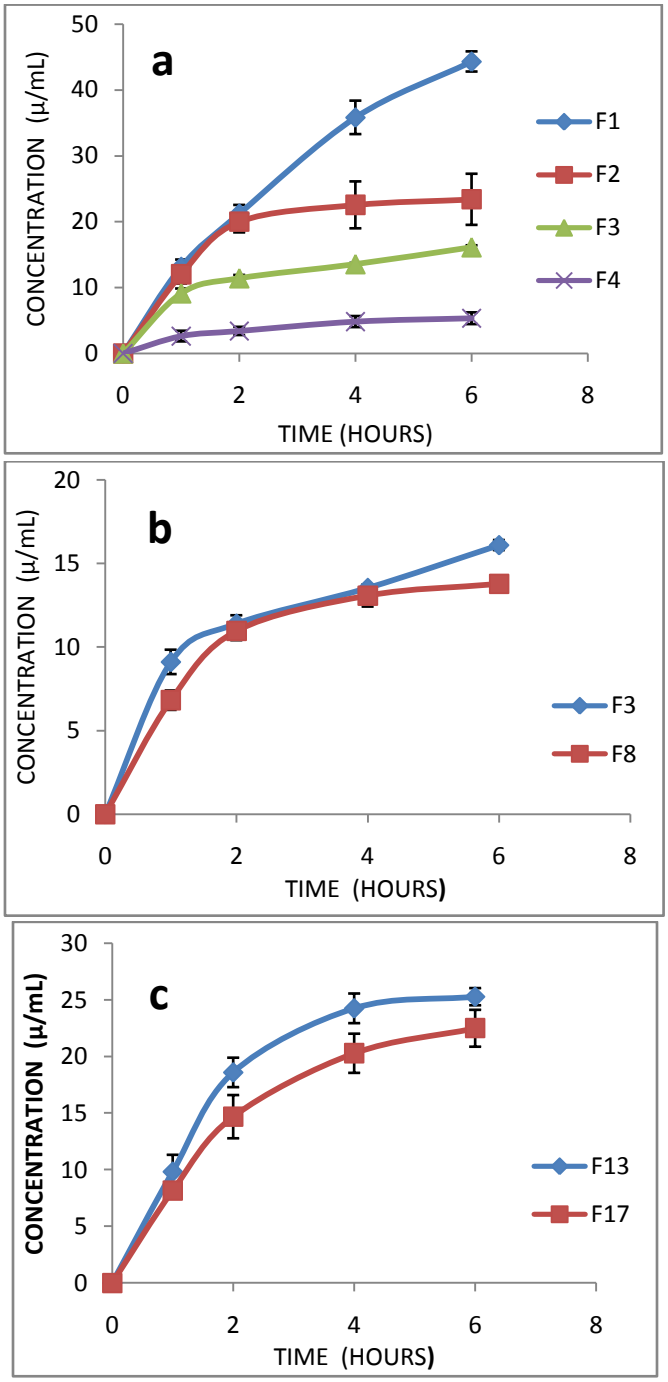


*Figure 3:* Release of formulations: (a) containing 20mg (F1), 15mg (F2), 10mg (F3) and 5mg (F4) of the drug; (b) containing 10mg of the drug: comparison betweenF3 (high molecular weight polymer) and F8 (low molecular

weight polymer); (c) containing 10mg of the drug: comparison between F13 (high molecular weight polymer) and F17 (low molecular weight polymer) both contain twice the mass of polymer.

**Release Kinetics**

As can be seen, for all formulations used in the release test, the best model for explaining drug release is the Higuchi Model. This is because the drug is dispersed in a matrix, and what controls the release is diffusion. Thus, the water enters the polymeric structure of the microparticles, dissolves the drug and it exits to the external medium by diffusion. The Higuchi model has a wide application in polymer matrix systems.

**Table 3**: Results of release kinetics

| Formulation | Zero Order Model ($R^2$) | First Order Model ($R^2$) | Higuchi Model ($R^2$) |
|---|---|---|---|
| Formulation1 | 0.935 | 0.311 | 0.973 |
| Formulation2 | 0.481 | 0.035 | 0.912 |
| Formulation3 | 0.540 | 0.072 | 0.947 |
| Formulation4 | 0.692 | 0.520 | 0.985 |
| Formulation8 | 0.556 | 0.148 | 0.942 |
| Formulation 13 | 0.701 | 0.192 | 0.961 |
| Formulation 17 | 0.789 | 0.271 | 0.983 |

**Conclusion**

The process of encapsulation of Piroxicam using UltraTurrax was successful in the formation of microparticles with high encapsulation efficiency, spherical shape, and smooth and regular surface. The microparticles developed in this work succeeded in prolonging the release of the drug, without releasing its totality. Among the formulations produced, F3 is best suited for future *in vivo* release studies using rats with chronic inflammatory diseases because it has high encapsulation efficiency, high content and slow release.

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