El objetivo de este estudio es caracterizar la liberación de calcio, fluoruro y fosfato de resinas de intercambio iónico cargadas con dichos iones. Se han estudiado también esta liberación en mezclas de resinas de los diferentes iones en estudio. El objetivo final es evaluar estas resinas como fuente de iones calcio, fluoruro y fosfato para la remineralización de tejidos organominerales.

Se ha caracterizado el intercambio iónico calcio/sodio, calcio/sodio-potasio y fluoruro/cloruro. Se ha estudiado como afectan a estos intercambios los parámetros de pH, temperatura, tamaño de partícula, composición de la disolución externa y la encapsulación de las resinas en una matriz de chicle comercial.

Para conseguir resultados reproducibles se ha desarrollado una técnica para estudiar los procesos de intercambio iónico en resinas encapsuladas en chicles. Este método consiste en renovar la superficie de las muestras simulando una masticación, de manera que la disolución externa entrara en contacto con toda la muestra.

Los estudios de adsorción/desorción se han llevado a cabo en discontinuo utilizando un sistema como el mostrado en la figura 1:

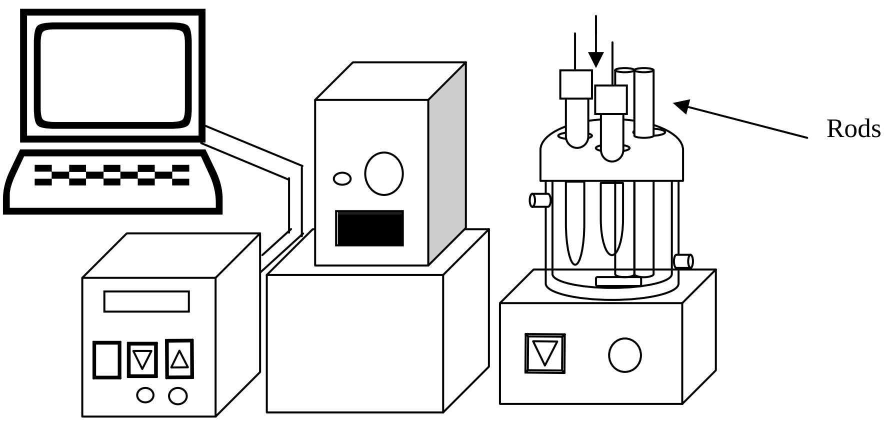

Figure 1: Experimental system

Posteriormente se ha realizado el estudio de una mezcla de resinas de calcio, fluoruro y fosfato en una relación 2:1:3 llamada NMTD (Nuevo Material de Tratamiento Dental). Con el fin de estudiar el comportamiento de esta mezcla de resinas en un chicle comercial se han estudiado el efecto de los diferentes aditivos que contienen los chicles comerciales sobre la liberación de los iones

El siguiente paso ha sido estudiar la liberación *in vivo* de los iones de la mezcla NMTD encapsulada en un chicle comercial. Diferentes individuos han masticado el chicle durante 20 minutos, obteniéndose una muestra de saliva a los minutos fijados. Los resultados muestran como la concentración de calcio, fosfato y fluoruro en la saliva aumentan debido a la presencia de la mezcla de resinas NMTD.

Para evaluar las resinas de intercambio iónico como agentes remineralizantes se ha llevado a cabo un estudio *in vitro* para cuantificar el efecto sobre el esmalte dental al cual se le ha provocado una lesión o caries. La variación en la dureza del esmalte, la absorción de fluoruro y el porcentaje de mineral dental en el esmalte son los parámetros estudiados.

Se han estudiado las diferentes resinas, mezclas de dichas resinas y muestras encapsuladas en la matriz de chicle. Los resultados más representativos muestra como las resinas de intercambio iónico cargadas con fluoruro, calcio y fosfato son fuentes idóneas de dichos iones para la remineralización del esmalte dental. De la misma manera, las resinas mantienen este efecto remineralizante sobre el esmalte cuando están encapsuladas en chicles comerciales. Por este motivo, la aplicación de estos productos es muy sencilla y fácil que pueda llegar al consumidor final.

I.1 SUMMARY

Ion-exchange processes have become one of the most important and studied fields in chemistry due to the amount of possible applications to the industry. Although the ion-exchange science has been studied since the 19th century, many of the processes are still unknown. In most of the cases, the specific study should be analyzed in an independent way.

The aim of this study is to characterize the release of calcium, fluoride and phosphate from mono-component ion-exchange resins, binary and ternary mixtures. The final goal of this study is to evaluate these resins as suitable sources of calcium, phosphate and fluoride for the remineralization of organomineral tissues.

Ion-release studies were performed to characterize the ion-exchange of calcium/sodium and calcium/sodium-potassium and the ion-exchange of fluoride/chloride. The effect of pH, temperature, particle size, composition of the external solution and capsulation of the resin in a chewing gum matrix on the release of individual ions was studied. The effect of all these parameters was studied afterwards in different binary mixtures of calcium and fluoride. These mixtures were largely analyzed since calcium and fluoride presented the most important interactions in the studied systems. For this reason, this part of the study focuses on two effects: that of calcium presence on the fluoride release and that of fluoride presence on the calcium release. Release analysis and thermodynamic and kinetic characterization were carried out for all systems in different conditions to illustrate the whole processes which take place.

In order to obtain reproducible results, a technique to study ion-exchange processes in chewing gum capsulated resins was developed. It was identified that Ion-exchange phenomena in such samples are surface processes. To study the ion release from capsulated resins, surface of samples should be renovated along the study. Simulating mastication with two glass rods, it is possible to put in contact all the gum with the solution with reproducible results for the corresponding ion release.

Two different ion-exchange resins loaded with different ions were studied. On the one hand, a polyacrylic ion-exchange resin loaded with calcium and sodium was evaluated. On the other hand, an anionic resin, of a polystyrene-based structure, loaded with fluoride, phosphate and chloride was tested.

Sorption/desorption studies of calcium and fluoride ions in free and capsulated ion-exchange resins were conducted in a discontinuous process using the system shown inFigure 1:

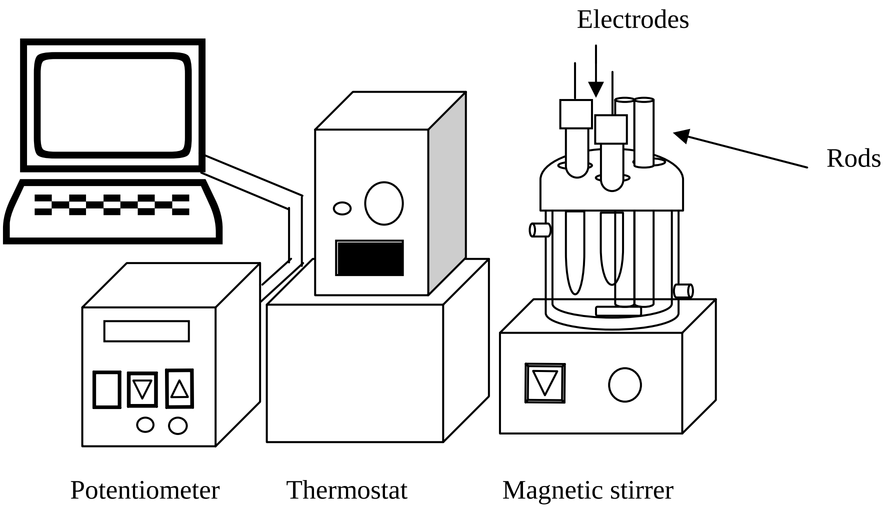

Figure 1: Experimental system

A thermostatic jacketed cell, where experiments were carried out, was kept to the studied temperature in each case. The response of the ion selective electrodes to the actual concentration of the ions was measured by a potentiometer provided with a software control that allows to periodically recording values of ISE potential, i.e, each minute, and then analyzing them.

Results showed that the sodium release was clearly higher than calcium release due to the affinity of the cationic resin to divalent ions. In the studied conditions, selectivity of anionic resin was different than the cationic case. Thus, both fluoride and chloride release are very fast, although only fluoride release achieve the release of the total fluoride content in the resin. In order to characterize kinetically these resins, two models were hypothesized: an intraparticular diffusion model and an interparticular diffusion model. The former model which is usually valid for resins with a small particle size considers that the rate-limiting step of the reaction is the intraparticular diffusion. The latter assumes that the rate-limiting step is the interparticular diffusion. Both models were applied and data fitted both of them.The interparticular diffusion model becomes more appropriate in the studied conditions with the increase of particle size. On the other hand, high difficulties were found to characterize anionic resins due to the quick release that they have presented in the studied conditions.

Resin selectivity did not change when ion-exchange resins were capsulated in a chewing gum matrix. Kinetic curves for the encapsulated resins showed two different effects. Thus, in the first minutes, reaction rate was lower than that obtained for free resins and it was attributed to a humidification step of the chewing gum. After this step, the rate increased up to the values obtained for free resins.

Results obtained in these experiments also showed that temperature, size of particle and encapsulation affect only to the kinetics of the process. The rate of the exchange was lower when both temperature was lower, the size of particle was higher and the sample was capsulated into a matrix. The effect of particle size was only observed in the cationic releases. Again, the quickly anion release make difficult to observe differences in the study of the mentioned effect. pH also affects only to calcium release due to the acid/base properties of cationic resin. When the pH was lower the release of calcium was higher since the carboxylic groups are very selective to protons.

The most important variation in the release of the studied ions was observed in the effect of fluoride in the calcium release and the effect of calcium in the fluoride release. Depending on the ratio of these ions in the studied samples, the release of the ions was enhanced or reduced. One of the observed phenomena was the supersaturation of solutions formed when the mixtures of resins contained a higher ratio of the fluoride-loaded resin. This phenomenon occurs because of the interaction among the ions of the solution and those on the resin particles in suspension. This supersaturation of the solutions provokes that the calcium release is higher than expected in these types of mixtures.

Another studied parameter was the composition of the external solution and, particularly the presence of gastric mucin. This organic mixture containing glycoproteins affect the release of ions, especially that of calcium. Gastric mucin weakens the interaction between functional groups of the resin and calcium ions. For this reason, the release of calcium from calcium-loaded resin or mixtures with a higher ratio of calcium-loaded resin is higher when gastric mucin is in the medium. The barrier-effect of the gastric mucin which affects the interaction of the resin with calcium, also affects the supersaturation phenomenon blocking the interaction among the particles of resin and the ions.

A mixture of resins loaded with calcium, fluoride and phosphate with a 2:1:3 ratio called NMTD was studied. In order to obtain a commercial chewing gum containing NMTD, experiments were also conducted capsulating the mixture of resins in a related gum matrix, which contains different kind of additives of commercial chewing gums. Results showed an acceptable release for all the ions and the capsulation of the resin did not affect the equilibrium of the ion-exchange process, while kinetics was clearly affected. Reaction rate drastically decreases when the resins is capsulated, but the presence of the typical additives and the subsequent reduction of the gum matrix content, which is the diffusion barrier, provokes an increase of the ion release and allows to achieve the results of the non-capsulated resins. Resins also showed a buffer effect of the solution stabilizing the pH at 5.5 from acidic media, which is very appropriate to their possible oral care applications.

In vivo study was carried out with four panelists, who chewed different kind of gums containing the mixture of resins NMTD for 20 minutes with periodical withdrawal of saliva samples at specified times. After 20 minutes, panelists stopped chewing the gum and four additional saliva samples were collected at specified times. Blanks of chewing gum without resins were also tested. The study was performed by testing different chewing gum samples of different nature and additives. In all tests, the concentrations of calcium, phosphate and fluoride in saliva were determined. Results of the blanks showed that initial concentration of the studied ions in saliva were in the ranges 100-200 ppm for phosphate, 0.3-1.5 ppm for fluoride and 40-75 ppm for calcium. The same tests showed that phosphate ion concentration decreased while the panelists were chewing the gum and, only when they stopped chewing, the ions concentration reached the initial parameters. When gums contained the mixture of resins loaded with fluoride, calcium and phosphate, the ion concentration increased significantly. Phosphate ion showed an increase of 50-150 ppm in the first minutes of the test, which represents an increase of 50-75 %, plus the compensation of the natural decrease of the concentration when chewing; calcium showed an increase of 50-200 ppm, which represents an increase between 100 % to 400 %; finally, fluoride showed the most significant increase (to 10 to 50 ppm), since the initial concentration was very low. Results showed that the chewing gums containing the mixture of resins increased the concentration of ions in saliva and, thus, these ions are available to promote remineralization.

In order to evaluate the ion-exchange resins as remineralizing agents, an *in vitro* pH cycling remineralization/demineralization model[1] was used to study these products. Enamel hardness changes, fluoride uptake and volume percentage mineral were the studied parameters.

Mixtures of resins loaded with fluoride, phosphate or calcium ions were tested using the specified model. The use of ion-exchange resins allows keeping calcium, fluoride and phosphate in the same container with absence of reaction because the ions are located inside the macromolecular net of the resin. Results showed that ions were available to carry out the remineralization process. Therefore, ion-exchange resins could be considered as an ion source. It was also observed that fluoride ions are the most important remineralizing agent, as enamel hardness increase was higher than with other ions. In this study, it was observed that the simultaneous presenced of calcium, phosphate and fluoride promotes both enamel hardness increase and fluoride uptake to be higher than those for monocomponent or binary mixtures of resins with similar percentages of fluoride ion. When the ion-exchange resins were capsulated in chewing gum matrices, the release of ions decreased and, therefore, remineralization effect was lower. Nevertheless, this release was higher when the percentage of fluoride in the resin mixtures was higher. It was also higher when the chewing gums contained the current additives of a commercial chewing gum. In this way, these additives enhance the release of ions from the capsulated resins.

[1] White D.J (1987): Reactivity of Fluoride Dentifrices with Artificial Caries, I. Effects on Early Lesions: F Uptake, Surface Hardening and Remineralization, *Caries Res.* 21:126-140