

## ***In vitro* transdermal delivery of caffeine-loaded alginate particles**

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### **Introduction**

Encapsulation technique has emerged a few years ago as a promising technology for new drug delivery systems. The production of alginate microspheres via internal gelation offers a method of encapsulation a variety of biologically active agents including drugs [1], proteins [2] and enzymes [3], among others compounds.

In this study, alginate microspheres were prepared by emulsification/internal gelation technique. The purpose of this study was the improvement of absorption of caffeine through an *in vitro* permeation model. This carrier will be applied as carriers for anticellulitic treatment.

In our study, the polymer chosen was alginate. Alginate is a natural polysaccharide found in brown algae and used in the food and pharmaceutical Industries. Alginates have been successfully employed as a matrix for the encapsulation of drugs, macromolecules and biological cells [4].

### **Material and methods**

*Preparation of alginate particles:* A 2% (w/v) sodium alginate solution was prepared with caffeine at 1% (w/v). A suspension of CaCO<sub>3</sub> at 5% (w/v) was added to the alginate solution and dispersed at 400 rpm into 50 mL of paraffin oil containing 1.5 mL of Span 80. 15 min later, 20 mL of paraffin oil containing 300 µL of acetic acid were added to the w/o emulsion in order to solubilize calcium salt and stirring continued for 30 minutes. Microparticles were recovered using acetate buffer at pH 4.5 and centrifugation cycles [4]. A gel and cream containing caffeine at 1% were also prepared.

Viscosity of the caffeine gel and the gel without caffeine were measured by a viscometer.

*Morphological and particles size analysis:* Morphology was determined by optical microscopy. Size distribution of microparticles was determined by laser diffractometry with a size range from 0.02 to 2000 µm. Particle size was expressed as volume mean diameter (µm). Polydispersity was determined by the SPAN factor [4].

*Encapsulation efficiency:* The encapsulation efficiency was calculated by indirect method measuring the absorbance at 273 nm of the non-encapsulated caffeine. The encapsulation efficiency of the caffeine was then calculated from the difference between the total free caffeine and the initial amount of the drug. The other method that we calculated the encapsulation efficiency was by dissolving the microparticles with a solution of sodium citrate in pH 7.4 phosphate buffer. Then, the solution was centrifuged and caffeine in supernatant was quantified at 273 nm.

*In vitro release study:* The *in vitro* skin permeation studies were performed on Franz diffusion cell using silicone as permeation membrane. The profile of *in vitro* skin permeation was compared between caffeine gel, caffeine cream, and microparticles of caffeine prepared by emulsification/internal gelation technique.

**Results:** An encapsulation efficiency of 51% was obtained. The morphology of microparticles was determined. Particles were round as seen in Figure 1 with a mean diameter of 45 µm (Figure 2). SPAN factor was 2,014. The result of the viscosity of the caffeine gel was 212 cP and the gel without caffeine 126 cP.

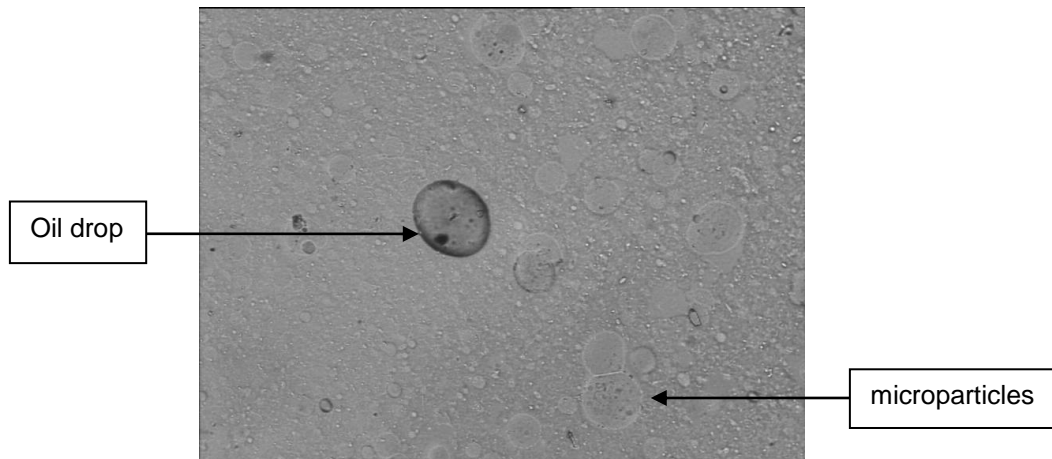
The results of the *in vitro* skin permeation performed by Franz diffusion cell revealed that microencapsulation of caffeine by emulsification/internal gelation method can be an alternative for the transdermal delivery of this drug.

**Discussion:** Optimization of drug delivery through human skin is important in current therapies. Polymeric microparticles can be considered as promising drug delivery systems since they demonstrated biocompatibility with tissue and cells, singular properties and subcellular size. Herein, the emulsification/internal gelation technique offers several advantages over other conventional methods, and shows a great promise in the development of encapsulation of drugs. This study confirmed that this technique successfully produced smaller particles with medical and pharmaceutical applications and may be applied to other drugs.

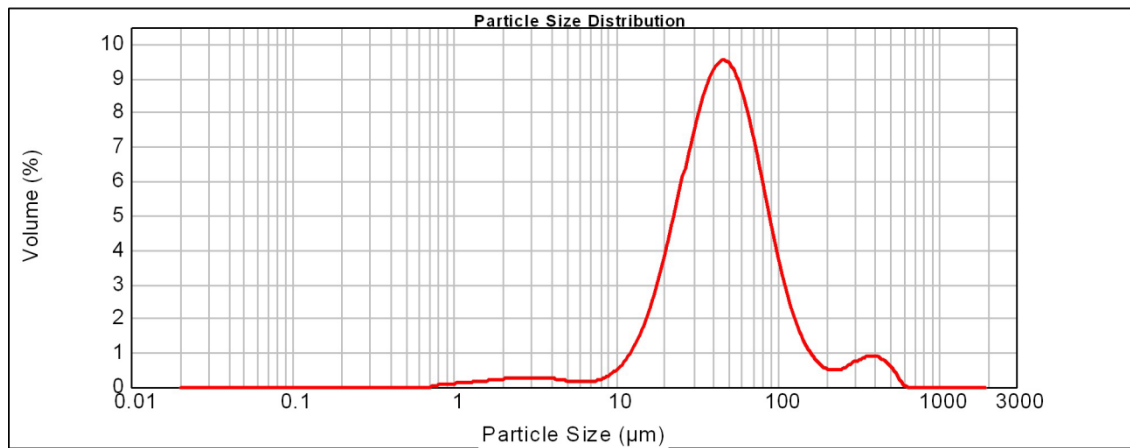
## References

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## Figures



**Figure 1** - Photograph of alginate particles.



**Figure 2** – Particle size distribution using Fraunhofer model.