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## PREPARATION OF SPRAY-DRIED MICROSPHERES CONTAINING KETOPROFEN: STUDY OF THE TECHNOLOGICAL PARAMETERS

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Ketoprofen (KP) is a non-steroidal anti-inflammatory drug (NSAID) widely used in chronic therapies for the treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. It is characterised by a short half-life ( about 1-2 h) and like other NSAIDs, ketoprofen has been found to cause local adverse effects in the gastrointestinal tract, in particular it was reported on the erosive action of NSAIDs on the gastric mucosa. As many other NSAIDs, it is a good candidate for the preparation of controlled drug delivery formulations (Giunchedi et al 1994).

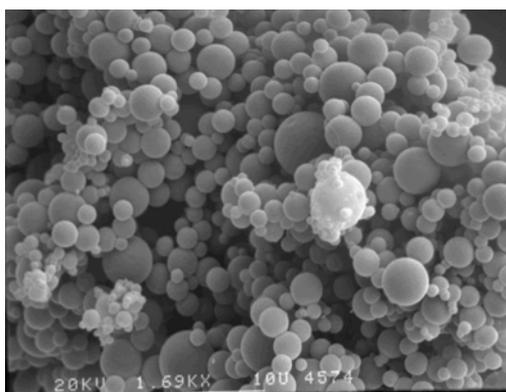
The purpose of this work was the preparation of spray-dried microspheres containing ketoprofen, using Eudragit polymers (polymethylmethacrylates) and the study of the influence of the preparative parameters on the characteristics of the microparticles obtained.

Microspheres were prepared by spray-drying of a solution containing KP and Eudragit RS-100 and RL-100 (50:50 ratio) in methylene chloride. The drug to polymer weight ratio was 1:3: an excess of polymer is necessary to obtain the particles (Gavini et al. 2003).

Eight batches were produced by changing preparative parameters such as inlet temperature, the peristaltic pump and the aspirator speeds. The particles were characterized in terms of drug content, particle size (laser diffractometry) and morphology (Scanning Electron Microscopy, SEM). The effect of the drying temperature on the properties of the microspheres was evaluated drying the particles at 30 and 20°C. The influence of the way of storage was also studied in opened and sealed vials made by glass or plastic. The effect on the microspheres morphology was observed after 15 and 30 days.

The results obtained show that the spray-drying technique is suitable to produce microparticles of KP based on a mixture (50:50) of Eudragit RS-100 and RL-100 regardless the instrumental parameters employed. They are spherical with smooth surface and no drug was revealed outside the microspheres (Figure 1). Nevertheless the parameters can influence the amount of the solvent residue in microspheres which can induce, especially in the sample sealed in the vials (both plastic and glass containers) a remarkable modification of the microsphere morphology due to its plasticizing effect. Moreover the stability of the particles depends on the temperature of drying: in fact temperatures  $>$  of  $25^{\circ}\text{C}$  determine a morphology modifications due to the initial fusion process of the polymers.

**figure 1** SEM picture of spray-dried microparticles (magnification 1,69 KX)



## References

- [1] Giunchedi P., Conti B., Maggi L., Conte U., 1994. Cellulose acetate butyrate and polycaprolactone for ketoprofen spray-dried microsphere preparation, *Journal of Microencapsulation*, 11, 381-393
- [2] Gavini E., Sanna V., Juliano C., Giunchedi P., 2003. Compressed biodegradable matrices of spray-dried PLGA microspheres for the modified release of ketoprofen. *Journal of Microencapsulation* 20, 193-201.