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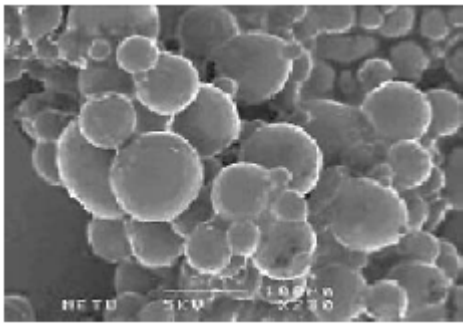

Fig. 1 SEM photograph of drug loaded chitosan microspheres.

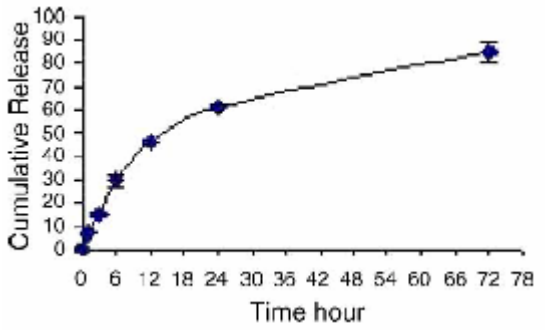

Fig. 2 Release profile of Alendronate sodium from chitosan microspheres.

The encapsulation efficiency of AS microspheres and the average particle size of the microspheres were found 3.3% and 109.28 ± 0.63. respectively. SEM photos revealed that microspheres were homogenous and had a spherical surface (Fig. 1). Release studies were carried out on chitosan microspheres in 0.1 M pH 7.4 sodium citrate solution and it was observed that the 85% of AS had been released from microspheres on the third day (Fig. 2). Prolonged release of AS from chitosan microspheres was observed during *in vitro* release studies. This formulation might be promising for the treatment of osteolysis in orthopaedics.

[1] Ezra. A., et al.. 2000. Adv. Drug. Deliver. Rev. 42, 175-195.

[2] Arica, B., Calis. S., Kas, H.S., Hincal, A.A., 2002. In: Muzzarelli, R.A.A., Muzzarelli, C. (Eds.), Chitosan in Pharmacy and Chemistry. Atec, Italy, pp. 71-76.

PO-56

Novel instrumentation for the design of microspheres for chemoembolization

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The therapeutic efficiency of embolization towards tumoral stuructures is improved by addition of a chemotherapy. The stopped blood flow at the embolization site lead our team to couple drugs to microspheres designed for embolization, taking advantage of the mainly diffusive mass transfer conditions to provide high local concentration and prolonged release of drugs. A critical issue in the manufacturing of drug delivery systems designed for parenteral route is the lack of guidance focussing on *in vitro* release apparatuses. Therefore, we designed a novel *in vitro* apparatus, modelling the particular hydrodynamic conditions encountered at the embolization site. We transformed porous microspheres suitable for embolization into drug delivering microspheres through impregnation by alginate [1]. These novel microspheres were able to transport various hydrophilic tracers (indomethacin [2], FITC-dextran) with molecular masses ranging from 102 to 105 Da, highlighting their high potential as a drug delivery platform. Furthermore, impregnation provided a sustained release of the transported compounds in an *in vitro* continuous flow release system. Release from these microspheres at the embolisation was studied using the novel *in vitro* release apparatus, the "T"-apparatus. Controlled diffusive-convective process similar to mass transfer conditions encountered at the embolization site were reproduced [3], allowing the analytical study of release kinetics. Our novel drug delivering microspheres displayed drug releases over long time scales, highlighting their efficiency as prolonged-release microspheres.

[1] Boudy, et al., 2002. World Patent 0,241,928.

[2] Chretien. et al., 2004. J. Control Release 96, 369-378.

[3] Amyot, et al., 2002. Int. Com. Heat Mass Transfer 29, 623-632.

PO-57

All-trans-retinoie acid microspheres: Preparation and *in vitro* characterization

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Retinoic acid (RA), a vitamin A acid, regulates differentiation, proliferation of epithelial tissues, all important biological process such as growth, development, differentiation. reproduction, morphogenesis. metabolism, homeostasis. It has been used in dermatology, hematology, cancer research and therapy and embryonal development [1]. Antiproliferative effect of RA for retinal pigment epithelium has been reported [2]. It has been proved that RA is effective to reverse the squamous metaplasia in conjunctiva, caused by dry eye syndrome [3.4]. Poly (lactic-co-glycolic acid) (PLGA) microspheres of retinoic acid were prepared by using modified emulsion/solvent evaporation technique. PLGA (50:50) were used in two different viscosities (0.17 and 0.39dl/g). Polyvinyl alcohol or polyvinyl alcohol-sodium oleat mixture (4:1) were the emulsifying agent at the concentration of 0.5 or 1.0% (w/v). For this purpose eight different formulations were repared. The particle size range was obtained

between I and 2 μm. Microspheres were smooth and spherical in shape as determined by SEM photographs.The yield of microspheres was 50-75% and the encapsulation efficiency was about 45-75%. *In vitro* release studies showed that RA release from microspheres lasted for 11-13 days. The released amount of RA was assayed by HPLC. *In vitro* data of the present study showed that polymer viscosity, emulsifying agent type and emulsifying agent concentrations are the critical parameters affecting the release of RA from the PLGA microspheres.

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[2] Li, A., et al., 2002. Invest. Ophthalmol. Vis. Sci. 44, 996-1007.
[3] Tseng, S.C., et al., 1985. Ophthalmology 92, 717-727.
[4] Selek, H., et al., 2000. Eur. J. Ophthalmol. 10 (2), 121-127.

PO-58

Comparison of dissolution profiles of two commercially available trimethoprim/sulfamethoxazole tablets by a model-independent method

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During the development of a medicinal product a dissolution test is used as a tool to identify formulation factor that are influencing and may have crucial effect on bioavailability of the drug. In addition, a dissolution test is used in the quality control of a scale-up and of production batches to ensure both hatch-to-hatch consistency. It can also be used to support the bioavailahility of a new product, the bioequivalence of an essentially similar product. The objective of this study was to investigate the influence of dissolution medium on the *in vitro* release of trimethoprim/sulphamethoxazole from two commercially available tablet products. Dissolution studies were conducted in USP Apparatus 2 (paddle method) with twelve replicates. Three different buffers (pH 1.2. 4.6 and 6.8) were used as the dissolution medium and the paddle rotation speed was kept at 50 rpm. In all experiments, 5ml of dissolution sample was withdrawn and replaced with an equal volume of fresh medium to maintain a constant total volume. Dissolution profiles were compared using two model-independent parameters: the difference (f1) and similarity (f2) factors. According to the guidelines, fl values up to 15 (0-15) and f2 values greater than 50 (50-100) ensure the equivalence of the two curves. Based on the f1 (3.1) and f2 (72.8) values, only the dissolution profiles of trimethoprim obtained at pH 1.2 medium was considered similar. In all other conditions, release profiles were dissimilar. Regardless of the dissolution medium, dissolution profiles obtained for sulfamethoxazole were different (f1 > 25 and f2 < 37 for all mediums). All these results indicate that dissolution studies are not sufficient for demonstration of similarity of these tablet formulations and further *in vivo* studies are required.

PO-59

Drug-excipient interactions for a new positive inotropic agent

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PST 2744 ((5alpha)-androstane-3.6.17-ti-ione 3-[*O*-(2-aminoethyl)oxime| hydrochloride)) is an inhibitor of the Na^+/K^+ ATPase enzyme. Currently this compound is under clinical development as a new positive inotropic agent. In anticipation of the possible development of a freeze-dried formulation a compatibility study was carried out between the drug-molecule and the principal excipients that are utilized as bulk-agents, as stabilizing agents during freezing and drying stages and as tonicity agents.

Physical mixtures with PST 2744 were prepared with these excipients and DSC and IR analyses did not show drug-excipient interaction phenomena. In other words, all of the excipients considered are compatible with PST 2744. Subsequently the same excipients were added to PST 2744, dissolved in water. These solutions were lyophilized and DSC and IR spectra analyses performed. Interaction phenomena were different for the various excipients studied. For the purpose of identifying the best excipient to utilize as bulk and stabilizing agent the lyophilizates were subjected to thermal stress and the product stability was finally verified using HPLC analysis [1].

[1] Akers, M.J.. 2002. Excipient-drug interactions in parenteral formulations. J, Pharm. Sci. 9). 2283-2300 (review).

PO-60

Separation of propranolol enantiomers using β- and γ-cyclodextrins as solid membrane additives

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The aim of this work is to evaluate the ability of β- and γ-cyclodextrins (CDs) to selectively complex one of the enantiomers of propranolol (PRO). With this purpose, phase solubility studies were carried out with increasing