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water was used. Granules composed of model drug (acyclovir, lactose, pentoxifylline) and binder (HPMC, PVP) have been analysed. The aim of our work was to find out the correlation between the spreading coefficient *(S),* the friability and the true density of granules. To calculate the spreading coefficient values, it is necessary to determine the surface free energy of solids ($Y_S$). This determination is possible with contact angle measurement (Wilhelmy plate technique). Surface free energy was calculated according to Delia Volpe. Considering calculated spreading coefficient values, a prediction was made, that granules with PVP have better quality (lower friability) than granules with HPMC. Results show good agreement with this prediction. We also predicted, that friability of pentoxifylline granules with both binders will be the lowest in comparison with other two model drugs. But really better granules (with very low friability) were obtained only when greater amount of water for granulation was used. Friability decreases with higher binder concentration and there is also connection between low friability and low true density of granules. Our previous work has shown, that for fluid bed granulation the prediction of optimum binder with spreading coefficient is possible. It is clear now, that this is possible also for classic wet granulation processes, but other parameters such as, for example, binder concentration and water amount, have also major influence on the granules quality.

**PO-84** THEOPHYLLINE IN A PERORAL CR DRUG FORM

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Polymers forming viscous barriers around retardets reliably control liberation of the active substance in CR (controlled release) drug forms.

The matrix-type retardets, generally more favourably evaluated in comparison with the reservoir form may, in addition to other technologies, be also formed by direct pressing of well-deformable and cohesive blends. Such blend may contain Aerosil 244 and calcium phosphate, easily mixable with Carbopol 97 IP. Addition of the necessary amount of magnesium stearate will provide for good pressing in the presence of theophylline. The pressed CR matrix form can be evaluated from functional aspects by determination of the radial strength (disintegration) and the ability to absorb water as well as buffers adjusted to gastrointestinal conditions. Matrices prepared in this work met the required criteria. Drug release determined by the standard basket method was used as the key evaluating method.

Carbopol, applied as the retarding polymer in the matrices allowed liberation of 60-70% of the drug in 6 h at 5-10% concentrations.

**PO-85** EVALUATION OF MATHEMATICAL DISCRIMINATORY TOOLS FOR DISSOLUTION TESTING

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This work estimates and discusses the analysis of data obtained for dissolution profiles under different media pH conditions using mathematical methods of analysis described by Moore and Planner (1996).

Moore and Planner describe two equations: (a) 'difference factor' (fi-equation) and (b) 'similarity factor' (f;-equation), which are frequently used as discriminatory tools for differences in dissolution profile of different pharmaceutical formulations.

In this work we used these formulas for evaluation of dissolution profiles of diazepam conventional tablets in pH of dissolution medium. In the period of time needed for dissolution (30 min), the sampling time-points were set-up to obtain profile, which was supposed to have different characteristics for the dissolution media of different acidity (range of physiological variations).

The results suggest that $f_2$-equation can be chosen as a tool in such kind of investigations.

**PO-86** FORMULATION AND IN VITRO CHARACTERIZATION OF CHITOSAN TREATED 5-FU LIPOSOMES FOR LOCAL APPLICATION IN BREAST CANCER

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5-Fluorouracil, a pyrimidine analogue, is an antineoplastic agent which acts as an antimetabolite to uracil. It is used alone or in combination with other antineoplastic drugs in the palliation of inoperable malignant neoplasms, especially those of the gastrointestinal tract, breast, liver, genito-urinary system, and pancreas. Fluorouracil is used topically in the treatment of solar or actinic keratosis and other tumours and premalignant conditions of the skin including Bowen's disease and superficial basal cell carcinomas. Whereas, 5-Fluorouracil (5-FU) is hardly absorbed from the skin. Therefore, the aim of this study is to improve release characteristics and increase the residence time within the skin 5-FU containing liposomes using natural polysaccharides such as chitosan as a gel base.

Liposomes were prepared essentially according to the lipid film hydration technique. An aqueous solution of 5-FU was prepared in pH 7.4 phosphate buffer. Free drug was removed by ultracentrifugation by washing pH 7.4 phos-

phate buffer. Chitosan gel base (2%) was prepared by dispersing chitosan in 1% lactic acide. Liposome suspension was then blended homogeneously with chitosan gel. This mixture was poured into glass cells. Glass cells were incubated at 37°C and 1 ml of solution was removed at various time points. Released 5-FU was determined spectrophotometrically at 266 nm.

The release of liposomal 5-FU from the chitosan gel followed a time relationship with about 40% of 5-FU being released from the chitosan matrix in 24 h. In the same period, about 80% of 5-FU being released from the matrix.

**PO-87** THE EFFECT OF RHEOLOGICAL BEHAVIOR OF THE FORMULATION ON THE RELEASE AND PERMEATION RATE OF THE ACTIVE SUBSTANCE

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The objective of this study is to investigate how different types of polymers at different concentrations affect the release and permeation rate of the active substance through synthetic membrane and intact skin, respectively.

A submicron o/w emulsion containing a local anesthetic substance, was investigated in presence and absence of different polymers, CMC, Carbopol 934P, PEG400 or PEG4000. Various concentrations of the polymers were used in order to produce different rheological behavior. The amount of drug, which passes through the membrane, was measured as a function of time, using static diffusion cells with either Silastic® sheeting 500-1 or guinea pig skin as membrane. The emulsion without polymer was used as reference. Rheological measurements were performed giving the viscosity and yield value of the formulations. Finally, theoretical values for diffusion coefficient and diffusion pathways were estimated and compared with the experimental data to discuss different diffusion models.

Rheological behavior of the formulation, other than Newtonian, affected the release rate of the drug significantly. Topical formulations require a certain consistency in order to result in good patient compliance. Theoretical estimation indicates that in order for a topical formulation to stay in place, a yield value of about 50 Pa is necessary when it is applied as a 5 mm thick layer. On the other hand, yield values ≥40 mPa are sufficient to prevent convectional movement of the droplets in the emulsion, and thus, decrease the release rate of the active substance. The permeation rate of the drug wa.s not affected in the same level by the rheological behavior of the formulation. However, a significant decrease in permeation rate was measured at viscosity ranges suitable for topical administration. This may of course be a limitation where a fast onset of action is required.

**PO-88** TEICOPLANIN A GLYCOPEPTIDE ANTIBIOTIC: STABILITY AND MICROBIOLOGICAL EVALUATION

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Teicoplanin is a recently introduced glycopeptide antibiotic used for the treatment of a variety of aerobic and anaerobic Gram positive infections. As the development of a biodegradable and implantable delivery system containing teicoplanin for the localized treatment of osteomyelitis which is an inflammatory bone disease was the aim, the stability of the antibiotic should be maintained during the implantation period. Advantages of localized biodegradable therapy can be stated as high local antibiotic concentration at the site of infection as well as preventing the need of the removal of the implant after the treatment. Therefore, in this study, the stability of teicoplanin was investigated by a short-term stability test. For this purpose, accelerated stability studies for a six month period were performed. During the stability studies, the temperature was kept at 40 ± 2°C and the relative humidity was 75 ± 5%.

Antibacterial activity of the samples was determined by broth microdilution method according to the National Committee for Clinical Laboratory Standards. *Staphylococcus aureus* ATCC 25923 was used as a reference strain. Results were expressed as minimal inhibitory concentration (MIC, μg/ml) values. To determine the growth inhibition zones of the samples, agar diffusion method was used. The samples were pipetted into the wells cut in the agar plates. The diameters of the inhibition zones were measured in millimetres.

At the end of the 3rd month of the study, 93.10% of the activity of teicoplanin was determined to be lost. An increase in MIC values was observed due to the time beginning at the 6th week.

**PO-89** EFFECTS OF STORAGE CONDITIONS ON THE PHYSICAL AGING OF POLYVINYLPYRROLIDONE: COMPARISON OF ENTHALPY RELAXATION AND POSITRON LIFETIME DATA WITH THE TENSILE STRENGTH OF TABLETS

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Physical aging in polymeric systems is the term used to describe the time dependency of changes in the behaviour of an amorphous polymer held at temperatures below the glass transition. Volume relaxation and enthalpy relaxation are