

enhancer (M). The results were described by *in vivo* and *in vitro* studies. *In vitro* we used the Mühlmann method and *in vivo* we used groups of 6 rats with weight near 120±10g. The contained in MET was counted on spectrophotometer UV/VIS Jasco V530 at 15, 30, 60, 90 min. ($\lambda=257\text{nm}$ for MET) (2). The three formulas of suppositories met the conditions of F.R.X concerning aspect, mass uniformity, melting characteristics and cantitative dosage. The kinetics of release and difusion of sodium metamizole displayed no significant differences between S and C formulas. The T formula had better results also *in vitro* and *in vivo*. In *conclusion*, the quantity of sodium metamizole which penetrated the biological membrane was higher when associating the penetration enhances for formulation T (90%), compared to standard sample M (79%).

P089

IN VITRO RELEASE OF BENZYL NICOTINATE FROM HYDROPHILIC GELSPopovici Iuliana¹, Braha Steriana¹, Miftode Alina Monica²¹Faculty of Pharmacy; ²Faculty of Medical Bioengineering, University of Medicine and Pharmacy Gr. T. Popa, 16 Universitatii str., 6600, Iasi, Romania

Romanian industry of drugs produces only one pharmaceutical dosage form, the ointment *REVULSIN* with 3% benzyl nicotinate in absorption vehicles containing 10% lanoline and 90% white petroleum, because the drug has lipophilic properties. The purpose of our research study was to establish the release behaviour of benzyl nicotinate from hydrophilic ointments, consisting of natural macromolecules like starch or semisynthetic ones like methylcellulose and sodium carboxymethylcellulose. The aim of this article was the formulation and *in vitro* release of benzyl nicotinate from three hydrophilic ointments in which the liquid drug was dispersed as an emulsion type o/w.

There have been formulated the following ointments which contained:

INGREDIENTS	FORMULATION (g)		
	1.	2.	3.
Benzylnicotinate	3	3	3
Starch	7	-	-
Glycerol	93	-	-
Methylparaben	0,2	0,2	0,2
Methylcellulose	-	6	-
Sodium carboximethylcellulose	-	-	4
Distilled water	to 100	to 100	to 100

All the formulations have been physically and chemically characterized, the obtained results concerning their: aspect, pH and degree of dispersion. The release rate of benzyl nicotinate from three hydrophilic ointments was determined through unspecific tests by colour reactions for some substances included in ointments using specific reagents. It has been measured the reaction zone (in mm) at different time intervals: 1, 5, 15, 30, 45 and 60 minutes, respectively, that is the time interval in which benzyl nicotinate acts upon the skin. The biggest capacity of benzyl nicotinate's release was manifested by the ointment with sodium carboxymethylcellulose, then by the ointments with starch and methylcellulose. The hydrogel with benzyl nicotinate and sodium carboximethylcellulose was clinically tested on 20 voluntary patients for the local treatment of rheumatic diseases, with good results. These results lead to the conclusion that benzyl nicotinate can be formulated in hydrophilic ointments which release rapidly the active substance and repulsive action begins to manifest immediately after application. In addition, the ointments are physiological and are removed easily from the skin because they are washable.

P090

OBTAINING AND CHARACTERIZATION OF HEDERAE FOLIUM SELECTIVE EXTRACTS

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The therapeutic properties of the *Hederae folium* well known in popular medicine are recognised by the modern medicine. With the purpose to obtain topical preparations which are supposed to treat the peripheral circulation disorders, cellulite and varicosity, this study has in view the obtaining and characterization of five selective extracts from *Hederae folium* rich in saponines. By extraction with selective solvents in various experimental conditions (pH, temperature) there were obtained five extracts. The extracts were then characterized by biological methods (hemolytic action) and tested for antifungal activity.

P091

SULFASALAZINE MATRIX COATING WITH LOW MW DL-POLY(LACTIC ACID)

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The use of biodegradable polymers in controlled release systems is a subject of extensive research today. Their importance does not lie only in the advantages that present against conventional materials but also that biodegradable polymers present a wide range of attributes, and one in particular, their biocompatibility, has been widely accepted. Towards this end polylactic acid (d-L-poly(lactic acid)) a low molecular weight polymer, roughly 2000, was used as a matrix and as a coating material for the matrix in order to study sulfasalazine release. In the first step the drug was added and mixed into a melt of polylactic acid, and then subsequently the mixture moulded into slabs (100mm diameter). In the second step the tablets, which were coated with the polylactic acid prepared by direct compression with a carver press. The polymers that were selected as excipients were Ethocel and Gantrez as well as a mixture of these. The matrix coating was prepared by immersing the tablets in a solution of polylactic acid in chloroform, not exceed 4-5% of the tablet weight. For the release study the tablet was immersed in buffer solution pH=7,4 and measurements were carried out at regular time using a UV-Vis intervals in spectrophotometer, which recorded drug release as a function of time. According to the results the release of sulfasalazine from polylactic acid matrices is completed within 8-10 days, depending on the quantity of drug present. Therefore it can be considered suitable for use in biomedical applications. Furthermost the matrix coating with polylactic acid delayed drug release, to a degree depending upon the matrix content of the drug but also from the recipient. Since the factors that influence the function of coatings are numerous, (e.g. coating thickness), it is obvious that more extensive study of the subject is necessary in order to achieve the best result.

P092
COMPARISON OF FATTY ACID PROFILE IN HEPATOCYTE MEMBRANE AFTER DIETARY SUPPLEMENTATION WITH N-3 OR N-6 POLYUNSATURATED FATTY ACIDS IN RATS

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Excessive amounts of n-6 polyunsaturated fatty acids (PUFA) and a very high n-6/n-3 ratio in the diet promote the pathogenesis of many chronic diseases, including cardiovascular disease, whereas increased levels of n-3 PUFA (a low n-6/n-3 ratio) have protective effects. *Objective* of this study was to compare the fatty acid profile in rat hepatocyte by n-6 or n-3 polyunsaturated fatty acids supplementation of diet. Wistar rats received either 3.3 g sunflower oil/kg of food or 7.5 g flaxseed/kg of food. Phospholipid fatty acid composition was determined by capillary gas chromatography in liver membranes. We found a different fatty acid profile in liver membrane between the two rat groups. Alpha linolenic acid (ALA) content was higher in flaxseed group as compared to sunflower oil group ($1.46 \pm 1.33\%$ vs. $1.3 \pm 1.33\%$) in liver membrane. Sum n-3 (ALA + eicosapentaenoic acid, EPA) was significantly higher in flaxseed group as compared to sunflower oil group ($2.63 \pm 3.06\%$ vs. $1.3 \pm 1.33\%$). Sum PUFA ($28.72 \pm 5.42\%$ vs. $23.84 \pm 9.30\%$), unsaturated index (101.42 ± 18.16 vs. 78.73 ± 26.28) and essential fatty acid index (1.63 ± 0.51 vs. 1.35 ± 0.78) were significantly higher in sunflower group. Dietary enrichment in flaxseed resulted in decreased n6/n3 ratio, (8.06 ± 2.46 vs. 21.09 ± 3.42). In *conclusion*, present work suggested that supplementation of n-6 PUFA or n-3 PUFA representing 1% of daily energy results in modifications of membrane fatty acid composition and decreased the n6/n3 ratio.

P093
RELEASE KINETICS OF BIOACTIVE SUBSTANCES FROM POLYMERIC NANOPARTICLES USING DIFFERENTIAL PULSE POLAROGRAPHY

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The growing use of nanoparticles as systems for controlled administration of bioactive substances lead to the development of analytical techniques for determining the quantity of the released drug. Unfortunately, the techniques that are currently in use are rather complicated, time consuming and usually not suitable for the release kinetics study of the entrapped compound. In the present work the differential pulse polarography (DPP) was used for the in-situ, non-destructive, monitoring of the released quantities of bioactive substances, such as pyroxicam and diazepam, from nanoparticles of poly(lactide-co-glycolide) (PLGA) and from poly(lactide-co-glycolide) copolymer with poly(ethylene glycol) (PLGA-mPEG). The respective polarographic calibration curves were constructed and the detection limits were determined. The possible influence of the polymeric particles on the polarographic signal was also studied. The release of the entrapped drugs from the nanoparticles was monitored with time and the results were compared with those obtained from the use of more conventional techniques. Some of the conclusions were: DPP can be used for monitoring the release of drugs from nanoparticles. The results of the proposed methodology were found to be in agreement with results obtained using more laborious and time consuming analytical techniques; The presence of the polymer does not influence the polarographic signal; The release kinetics depends on the lipophilicity of the bioactive compounds.

P095
SPECTROPHOTOMETRIC DETERMINATION OF LISINAPRIL IN TABLETS USING 1-FLUORO-2,4-DINITRO-BENZENE REAGENT

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