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Influence of Industrial Factors On The Dimephosphone Stability In Its Aqueous Solution

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The Dimephosphone (D) (dimethylic ether 1,1-dimethyl – 3-oxobuthylphosphonic acid) was synthesized in the Institute of Organic an Physical Chemistry named after A.E. Arbusov of Kazan Scientific Center of Russian Scientific Academy and was studied in Kazan State Medical University. The D is recommended by the Russian Pharmacological Committee for internal and external use in the form of 15% aqueous solutions as a remedy with antihypoxanthic, cytoprotective, radioprotective effects, which can improve tissues metabolism and increase the protective functions of skin and mucous membranes. The elaboration of new drug forms (DF) of the D is very actual because of it's unique complex of effects. Inspite of the stability of the D in its 15% aqueous solution, which is stable for 3 years without adding any stabilizer and any preservative, the presence in its molecular of two complex etheric groups can define the hydrolysis opportunity in the manufacturing process of DF. The estimation of influence of industrial factors-heating time (1,2,3, 4 hours) and temperature (45, 60, 75, and 98°C)-on the stability of D stability in an aqueous solution under the pH criterion (by potentiometry) and hydrolysis products content – monomethylic ether 1,1-dimethyl- 3-oxobuthylphosphoric acid (I) (by titrimetry). The influence of each factor was expressed calculating the force by the method of dispersion analysis of two-factors orthogonal complex and the combination of such factors (by the method of Snedecor) on the accumulation of (I): the heating time – 9,12%, temperature-82,72%. The opportunity of DF manufacturing with the D in an aqueous solution was established. For the receiving the stable DF of the D the manufacturing technology provides for the limitation of thermic influence on the preparation by the temperature conditions not exceeding 45°C.

The Possible Enhancement Mechanism I: An Investigation of Enhancer Activity of Capsaicin And Azone

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Capsaicin is one of the main alkaloids found in Capsicum species. It has some pharmacological effects. It is known as an antagonist to the substance P which is thought to be responsible for the joint inflammation. Capsaicin is also known to contract smooth muscles and it has an excitatory effects on thin, primary afferent neurons.

Azone is well known enhancer which increases the penetration of the penetrants through the skin by increasing lipid acyl-chain disorder in the structured lipids. Because of its very high partition to the lipids (the calculated value of log K_{oct}=6.28-7.82), it can stay amongst the skin lipid and it disrupts the lipid domains. It is noticed that the Capsaicin molecule has some similarity to that of Azone and the log K_{oct} values of the capsaicin were calculated with the value of 3.04-4.00. This value was thought to be good enough for Capsaicin molecule to stay among skin lipids like Azone.

The enhancer effects of Capsaicin were investigated using Franz type diffusion cells. Human cadaver skin was used as a membrane. Naproxen was chosen as a model drug. The penetration of Naproxen was determined using HPLC. The enhancer effects of Capsaicin was observed and compared with the results of Azone. The increased permeations were observed when the skin was pretreated with Capsaicin and Azone. The polydimethyl siloxan (PDMS) membrane was also used as an artificial model membrane. All the results were compared. As a result, Capsaicin was found to be quite capable enhancer for the skin. The possible enhancement mechanism was also discussed with current knowledge.

Enhancement of Solubility of Sulfamethoxazole By Complexation With Cyclodextrins

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Sulfonamides are bacteriostatic agents that are systematically used in treatment and prevention of bacterial infections. Even though their oral absorptions are good, as their solubility is low in GI fluids they particularly manifest bioavailability problems among individuals. In this study sulfamethoxazole was chosen as an active material which is the member of the sulfonamide group. In order to increase the solubility of sulfamethoxazole in water soluble carriers were prepared. The interaction between sulfamethoxazole and different types of cyclodextrins (α, β, and HPβCD) in solution was studied by solubility method. The molar ratios and stability constants of inclusion complexes were calculated from phase solubility studies. The solid dispersions were prepared by kneading and co-precipitation methods. The physical mixtures were also prepared for comparison. Inclusion complexation was confirmed by the results from the studies of X-ray diffraction, Differential Scanning Calorimetry and Infrared Spectroscopy. The rates of release of the active material from the resulting complexes were determined from dissolution studies using paddle method. In this study, the effects of additives which were added to the complexes and the stabilities of prepared complexes in different environments were also investigated. As a result of this study, it was found that solubility of sulfamethoxazole was increased by inclusion of cyclodextrins in the formulation.

An Electrical Device For Measuring Thickness of Hydrated Inserts

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Soluble ophthalmic inserts are composed of a water soluble polymeric support containing or not drug(s), the latter being incorporated as a dispersion or a solution in the polymeric support. The inserts can be used for topical or systemic therapy. In comparison with the traditional ophthalmic preparations (i.e. eye drops) the water soluble inserts present some advantages such as; increasing contact time and thus improving bioavailability, possibility of providing a prolonged drug release and thus a better efficacy, reduction of systemic side effects and thus, reduced adverse effects, reduction of the number of administrations and thus better patient compliance. They also offer of being entirely soluble so that they do not need to be removed from their site of application.

In this study, we intended to prepare ophthalmic inserts of indomethacin. Soluble ophthalmic inserts of this drug were prepared using water soluble polymers such as HPC, MC, HPMC and PVA by the film casting method. An electrical device for measuring thickness of the inserts was developed.

The electrical device consists of a micrometer, source power (12 V) and analog avometer (50 mA). The inserts were placed on the stainless steel plates and immersed in pH 7.4 buffer solution. Thickness of the hydrated inserts was measured by this electrical device at the selected time intervals for release studies. Thickness of the hydrated inserts was one of the most important factors affecting the release rate of the drug. The results obtained were compared with the release rate of the drug. Consequently, as the gel thickness of inserts increased, the release rate of the drug decreased.

Application of A New Cellulose Derivative For The Formulation of Prolonged Release Theophylline Encapsulated Granules

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A new water soluble cellulose derivative code named SCD-LVG prepared by etherification of alpha cellulose from a tropical edible wood pulp was employed as a prolonged release hydrophilic matrix for Theophylline encapsulated granules. The release of Theophylline from the encapsulated granules was studied in vitro in two different medium of pH 1.2 and 7.5. The performance of SCD-LVG as a prolonged release matrix for Theophylline was compared with that of carboxymethylcellulose (low viscosity grade), tragacanth and methylcellulose in the same experimental conditions. The result indicate that SCD-LVG exerted marked prolonged release of Theophylline at concentrations above 6% (w/w), and that Theophylline release from the polymer matrix was slightly faster in simulated intestinal fluid (pH 7.5) than in 0.1 N hydrochloric acid (pH 1.2). From release experiments carried out with different concentrations of SCD-LVG, together with mathematical treatment of the experimental data, it was noted that the swelling and erosion of the polymer matrix seem to be the most likely factors responsible for the overall rate of Theophylline release. The new cellulose derivative generally, was as good as tragacanth or methylcellulose or carboxymethylcellulose in prolonging the release of Theophylline from the encapsulated granules.

Stabilization And Control of Effervescent Tablets With Acetylsalicylic Acid

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Models of effervescent tablets with and without active compounds are studied. Come factors determining the stability of the formulations in humidity and high temperature conditions are followed.

In the achieved stable placebo formulation are included ASA and ascorbic acid.

An express control method is developed for following the free salicylic acid content in the process of obtaining and storage of the effervescent tablets.

Validation is carried out for the technological processes as well as for the control method.

Study of Dermatological Pharmaceutical Form With Protective Action Against UV And IR-Rays

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A dermatological composition for protection against the harmful influence of UV and IR-rays is formulated.

For this aim is selected an emulsion base type W/O with compounds for chemical and physical protection of the human skin.

The chemical absorption is realized by a filter, absorbing the rays from 280 to 320 nm. Physical protection is ensured by Bentonite and Zinc oxide for defraction of the rays from 200 to 400 nm and for protection of the skin from overheating.

The influence on the elaborated preparation on the normal physiological skin functions is studied.

Preformulation Study of Li-DL-Aspartate

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Initially, comparative toxicological and pharmacological investigations of Li-DL-Aspartate with Li-carbonate were carried out. The data showed the lower toxicity and higher antidepressant activity of Li-DL-Aspartate.

The following properties of the Li-DL-Aspartate were studied: bulk, tapped and true density, Hansner ratio, flow rate, angle of repose, residual moisture, particle size distribution, average diameter, compressibility, hygroscopicity, porosity, void volume, pKa, solubility in different solvents, pH. The O/W partition behavior at various pH- values of the polar phase and organic phases with different hydrophobic characteristics and ability to desolve water were investigated. Apparent partition coefficient (APC) were determined.

The diffusion study across artificial lipid barriers was carried out at pH-values simulated the physiological conditions. The stability against light, temperature, pH, and humidity were studied. The chemical stability was checked by means of TLC and IR-spectroscopy.

Reversed – Phase Liquid Chromatography For Evaluating The Distribution Behavior of Some Pharmaceutical Substances In Suppository Base Witepsol H_{15}-Phosphate Buffer System

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The aim of this study is to asses the potency of the high performance liquid chromatography (HPLC) for in vitro evaluating the distribution behavior of common drugs between the suppository base Witepsol H_{15} and the rectal liquid which is imitated by a phosphate buffer, pH = 7.2. The distribution coefficients (log W) of seven compounds- paracetamol, caffeine, diclofenac, propyphenazon, indomethacin, codeine and Phenobarbital- are determined by a reversed phase HPLC with C_{18} column. The capacity factors logk' are determined at a number of methanol-water mobil phases, pH = 7.2, with different percentage of methanol ϕ_{MeOH}. The apparent capacity factors at 100% water with pH = 7.2, named $logk_w'^{app}$, are derived from the linear regression of logk' and ϕ_{MeOH}. Using the correction for ionization $logk_w$- values are calculated. The lipophilicity of the compounds is assessed by the partition coefficients CLOGP and the distribution coefficients $CLOGD_{7.2}$, calculated for the n-octanol-water system. The correlation found between $logk'_w$ and CLOGP as well as $logk_w'^{app}$ and $CLOGD_{7.2}$ indicate that the HPLC is a suitable method for evaluating the lipophilicity of the compounds and can take part in SAR and QSAR studies. According to the correlation found between $logk_w'^{app}$ and log W, the parameter $logk_w'^{app}$ is suitable for evaluating the distribution behavior of the drugs investigated in the Witepsol H_{15}-rectal liquid system. Thus, the RP-HPLC method by its priority of rapid and reproducible experiment can replace the classical time-consuming "shake-flask" method for determination of logW. The logW-values indicate that the suppository base Witepsol H_{15} is appropriate for Phenobarbital, caffeine, codeine and paracetamol.

Liquid Uptake Into Unlimited Swelling Hydrogel Matrices

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The profiles of liquid uptake into neutral hydroxypropylmethyl cellulose and thermally pregelatinized starch matrix tablets and their mixtures were studied. The liquid content in the swollen hydrogels was gravimetrically measured. The influence of two aqueous solutions, i.e. i/0.1 mol/l HCl (pH 1.0), and ii/pH 6.8 phosphate buffer, was evaluated. The phosphate buffer uptake into all the systems studied was lower than that of the 0.1 mol/l HCl one. The polymer type and starch composition were the main factors that control the amount of the liquid sorbed by the matrices. To identify the liquid uptake mechanism, the penetration kinetics into matrices were analyzed using the empirical exponential equation which exponent describes a Fickian or anomalous uptake mechanism. In all the cases examined, the process of liquid penetration follows the classical Fickian diffusion-controlled mechanism.