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Investigations On Compatibility of The Dimephosphone And The Mephoprane With Auxiliary Substances

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The Dimephosphone (dimethyl ether 1,1-dimethyl-3-oxobthylphosphonic acid) and its structure analog-the Mephoprane were synthesized in the Institute of Organic and Physical Chemistry named after A. E. Arbusov of Kazan Scientific Center of Russian Science Academy. Such drug substances (DS) are uncolored transparent fluids. The compatibility of the Dimephosphone and the Mephoprane with auxiliary substances (AS) which are used in drug technology of drug forms (DF) of local action was studied. The suppositories with 1% of DS on the polyaethylenglycolic base and fat base were unstable in cause of violation of homogenity of surface and structure during the storage of DF. For the increasing the stability of DF of phosphonates the stabilizers with the different mechanism of action were studied: aerosyl and surface active substances, which were not able to protect aggregative unsteadiness of DF. The vaginal tablets can not be obtained because of nonmixing of phosphonates with AS, used in technology of vaginal tablets. The peculiarities of physico-chemical and technological properties of the Dimephosphone and the Mephoprane – fluid aggregative state of DS, aggregative unsteadiness in suppositories on hydrophilic and lipophilic bases, nonmoistening of powder-like AS and solubility in polar and unpolar solvents – determine of using in DF with fluid dispersion medium (solution, gel, foaming aerosol etc.).

The Possible Enhancement Mechanism II: Using Isolated-Perfused Rabbit Ear Model To Investigate The Skin Penetration of Naproxen And The Enhancer Effect of Azone And Capsaicin

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It has been proposed that Capsaicin induces the vasodilatation through the releasing substance P from sensory neurons. Substance P in turn, stimulates its receptors on endothelial cells of vessels causing a vasodilator substance release called EDRF.

It has been also demonstrated that vasodilatation enhances the skin penetration because of increased blood perfusion. The perfused pig ear model has been suggested for a better understanding of the skin penetration mechanism by maintaining vasculature and neuronal activities. On the other hand the chemical structure of Capsaicin was found to be similar to that of Azone which is known to be one of the enhancer used in skin penetration studies. Taken together, the isolated-perfused rabbit ear model was choosen for this investigation. The human cadaver skin samples were also used to investigate the lipid disruption effect of the enhancers (Azone and Capsaicin) and to make better comparison.

Naproxen was choosen as a model penetrant and the penetrated Naproxen was determined by HPLC. The vasodilator effect of Capsaicin and Azone was also investigated by recording the perfusion pressure. the vasodilator effects of Capsaicin and Azone and the vehicle were obtained and the potency order was obtained as Capsaicin>Azone>>Vehicle.

The enhancer effect of Capsaicin and Azone were determined. Capsaicin was found to be quite capable enhancer like Azone. The enhancement effects of Capsaicin and Azone were also determined using Franz type diffusion cells and the same enhancement trend was obtained.

In conclusion, altough the vasodilator effect of Capsaicin was demonstrated as with Azone, we put forward the idea that the Capsaicin may act an enhancer role by means of its chemical properties and lipophilicity like Azone. The vasodilator effects of Capsaicin was found not to be significant, because the dose of Capsaicin penetrated through the skin is relatively low in the isolated-perfused rabbit ear experiments.

The pH-metric LogK Calculation of Famotidine, Naproxen, Nizatidine, Ranitidine, and Salicylic Acid

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The octanol/water partition coefficient (K, often reported as logK) is a particularly useful parameter in Quantitative-Structure-Activity Relationships (QSAR). The logK is usually measured by the shake flask method, High Performance Liquid Chromatography (HPLC) or filter probe technique, but there has been growing interest in determining the parameter by potentiometry with a pH electrode. The latest technique uses the pK_a of the substance to determine log K.

The pH-metric technique typically consists of two linked titrations. The first titration is carried out in the aqueous phase over a pH range that encompasses the pK_a of the drug. The pK_a of the substance can be determined using half neutralization point of titration curve over it is particularly convenient to use the so-called "Difference curve". The difference curve (also called the formation curve or Bjerium plot) is a plot of n_H, the average number of bond protons (hydrogen ion binding capacity) versus-logH^+ for a single substance "X" in solution:

$$n_H = ([HCl] - [KOH] + nX - [H^+] + (Kw/[H^+]))/X$$

n = the number of dissociable protons introduced into the solution by the substance X
$Kw = [H^+][OH^-] = 10^{-13.75}$ at 25°C and 0.2 M ionic strength.

The titration is repeated after the addition of partition solvent, stirring vigorously through out to ensure equilibrium partition between the phases. A shift in pK_a to pK'_a is seen, the magnitude of which depends on the partition coefficient is given as follows:

$$K = (10^{(pK'a-pKa)} - 1)/r \text{ (for acids)}$$
$$K = (10^{(pKa-pKa')} - 1)/r \text{ (for bases)}$$
$$r = V_{org.}/V_{aqu.}$$

The pK_a's of famotidine, naproxen, nizatidine, ranitidine and salicylic acid were determined with the value of 6.209 ± 0.0782, 4.3 ± 0.0501, 6.261 ± 0.0194, 7.491 ± 0.0871, 2.95 ± 0.0145 respectively, using the Bjerium plot mentioned above. The logK values were calculated by repeating the titration with octanol. The log K values are given with the value of 3.95 and 2.23 for naproxen and salicylic acid in the literature. Therefore, naproxen and salicylic acid were selected as a known compound about their log K values. The logK values were also determined by HPLC and all the results were compared. Quite close results were obtained with these two techniques.

Study of The Correlation Between The Physical Mechanical Properties of Boluses And The Parameters of The Rotary Tablet Machine

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The influence of parameters of a rotary tablet machine on the physical mechanical indices of biconvex boluses with size 30 x 13 mm is studied.

Correlation between the thickness, the hardness and disintegration and pressure and the rate of rotation is found.

This study resulted in justification of parameters of the rotary tablet machine in the boluses tableting process.

On Some Problems In The Formulating of Tablet Dosage Form With Piroxicam-β Cyclodextrin

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Main problem in the formulation of tablet dosage form based on Piroxicam-β-cyclodextrin complex is to keep the entirety of the complex during the development process and storage.

The aim of this study is to investigate the influence of some of the excipients, solvents and the technological method.

The results obtained show that these factors posses determinative role for the amount of released Piroxicam above the admissible limits of 1%. The released Piroxicam was evaluated by DSC.

It was found that Povidon K 25 and Povidon VA 64 stabilize the complex regardless of the way of their incorporation in the tablet core. When the method of direct compression is used, the free Piroxicam is significantly above 1%-about 4-5%. At inclusion by wet granulation (as granulating agent) their stabilizing effect is in dependence of the type of the solvent. Better results were obtained by the use of purified water as a solvent, compared with ethanol 96%.

In these studies we used to make a formulation ensuring a stable oral solid dosage form with Piroxicam-β-cyclodextrin as an active substance.

Studies On The Commercial Salbutamol Sulfate Tablets In Turkey

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In this study, three different batches of two different companies salbutamol sulfate tablets from Turkish drug market were investigated.

For this purpose, the weight variation, content uniformity, diameter-thickness, hardness, friability, disintegration time and dissolution rate were determined for the commercial products.

The dissolution experiments were carried out with the Paddle Method (50 rpm) and the Basket Method of USP XXII. The distilled water was used as distillation medium at 37 ± 0.5°C.

The experimental results were evaluated according to the related monographs of T.F. 1974 and USP XXII. The dissolution rate data were assessed kinetically using a computer program.

Influence of Technological Factors On The Process of Extraction of Biologically Active Compounds From Bulbus Alii Sativi And Their Protective Activity On Tetrachloromethane Induced Liver Injury In Rats

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The aim of this study is to investigate the influence of several technological factors on the comparison of Garlic extracts. The hepatoprotective activity of standardized extracts is then studied using a model of tetrachloromethane (TCM) induced liver injury in rats.

The extraction condition (pH, solvent, temperature) depend on the specific physicochemical properties of the compounds to be extracted.

The extracts were standardized by diallyldisulfide (DADS) and diallylmonosulfide (DAMS) by HPLC. The protective activity was studied using extracts with high contents of DADS and DAMS in hepatotoxicity produced in rats. Our results suggest that the extracts exert a protective effect against TCM induced hepatotoxicity in rats judged by the system of cytochrome P450, malondyaldehyde contents as well as by total cholesterol concentrations.

Lipophilicity Parameters of Naturally Occurring Flavonols And The Retention In Reverse Phase Liquid Chromatography

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By applying a column and preparative chromatography the flavonol aglycons kaempferol, quercetin, isorhamnetin and the glycosides kaempferol – 3- glucoside, quercetin – 3- rhamnosylglucoside, quercetin – 3 – glucoside, isorahmnetin – 3- rhamnosylglucoside were isolated from the overground plant part of Bupleurum flavum Forsk. – Apiaceae. The flavonol glycosides of the plant extract were separated and identified by RP-HPLC followed by diode array detector as well as by high performance liquid chromatography interfaced with thermospray mass spectrometry. The results obtained by these techniques revealed the presence of quercetin – dirahmnoside, kaempferol – 3- glucoside, kaempferol – 3- dirahmnoside. Further, the lipophilicity of the identified compounds is assessed by the partition CLOGP and the distribution CLOGD coefficients calculated for the n-octanol-water system. It is founded a correlation between the capacity factors logk' obtained in the RP-HPLC system and the lipophilicity parameters calculated. The results indicate that the RP-HPLC method is useful for a rapid and accurate determination of the lipophilicity of the compounds investigated.

Selecting Suitable Conditions For Titrimetric Determination of Stabilizing Substances (Sodium Sulfite and Edetate Disodium) In Gel Basis of Local Dosage Form

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Sodium sulfite and edetate disodium were used as stabilizing substances in the gel basis.

Assay of edetate disodium was carried out complexiметrically. The difficulties were connected with eliminating the influence of lactic acid, precipitating after an alkalization of the solution with ammonia and impeding from reading the equivalent point. Suitable conditions were chosen: buffering the medium by urotropin and the indicator Tylenol orange.

Iodometric method was elaborated for sodium sulfite determination. A suitable analytical course for eliminating the influence of certain excipients impeding the analysis was selected.

The developed methods were validated.

Preformulation Study of Compatibility Between Bismuth Subcitrate And Tablet Excipients Using Differential Scanning Calorimetry

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In pharmaceutical preformulation work, studies of the interaction between drug and excipients in the solid state are obligatory. Excipients can affect the solid state stability of a drug either directly as a chemical reaction between the drug and the excipient or mostly, indirectly by sorption of moisture or catalysis.

Differential scanning calorimetry (DSC) was used to investigate the physicochemical compatibility between Bismuth subcitrate and number of commonly used tablet excipients.

Bismuth subcitrate was found to be incompatible with Mannitol and Sorbitol, but compatible with other studied excipients.

A stabilizing action of Povidon VA_{64} and Povidon K_{25} on Bismuth subcitrate was observed. The endoeffect of Bismuth subcitrate obtained in the physical mixtures with them is symmetrical and without decomposition.