EFFECT OF SOME COMMERCIAL ANTACIDS AND TEA DRINK ON THE IN-VITRO AVAILABILITY OF FRUSEMIDE

In this study, the dissolution rate of frusemide as a sparingly soluble diuretic, was determined in the presence of some commercial antacids. The effect of tea as a conventional drink on the in-vitro availability of the drug in the presence of the selected antacids was also investigated.

The obtained results revealed that, availability of frusemide was markedly affected in the presence of the selected antacids. The powdered antacids showed the most prominent effect while antacid tablets produced the lowest in this respect. Also, a marked reduction in the dissolution rate of frusemide was observed in the presence of both tea and antacids. The observed reduction in the dissolution rate of frusemide with these antacids may be attributed to the chemical interaction which was proved by IR, UV and TLC studies.

EFFECT OF SOME COMMERCIAL ANTACIDS AND TEA DRINK ON THE BIOAVAILABILITY OF FRUSEMIDE

The bioavailability of frusemide (FR) after oral administration of FR alone or FR with antacids or FR with antacids and tea drink has been investigated using rabbits. The urinary excretion rate was monitored and drug concentrations were compared. The results revealed that the drug bioavailability was markedly reduced in the presence of the selected antacids, viz. Neogelco and Semico suspensions, and Stomaclin powder. A significant reduction was recorded in both the total cumulative amount excreted over 24 h (P<0.05) and the excretion rate of the drug (P<0.01).

Tea drink was found to have an influence on FR absorption if taken concurrently with the tested antacids. With Stomaclin powder, tea drink significantly (P<0.01) increased the biological availability of FR compared to that obtained, with antacid alone, while such effect in case of Neogelco suspension was insignificant (P>0.05). With Semico suspension, however, tea drink significantly (P<0.01) reduced biological availability of FR.

Enhanced Percutaneous Absorption of ketotifen Fumarate through Rabbit Skin

Percutaneous absorption of Ketotifen fumarate (KT) in the gel formulation containing penetration enhancers was studied. The effect of ethanol (30%), menthol (M) (1, 2.5 & 5 %), and isopropyl myristate (IPM) (1, 5 & 10%) were investigated. The perfusion of KT via rabbit ear skin mounted in a Franz diffusion cell was evaluated. KT release was analyzed by UV-HPLC. Three groups of rabbits (6 rabbits in each group) were used in pharmacokinetic study. The first group was administered the solution of KT in pH 7.4 phosphate buffer by bolus injection (3 mg/Kg). The second and third groups of rabbits (formulae number 4 and 8 respectively) were exposed to topical application of KT gel (45 mg/2.55 cm2). The obtained results showed that menthol is the most potent enhancer for KT from gel formulations. The fluxes obtained were 17.4, 195.4 and 430.13 ?g/cm²h when menthol is added to the gel in concentration of 1, 2.5 & 5% w/w, respectively. Isopropylmyristate, in concentration of 1, 5 & 10% w/w, increases KT flux with subsequent increase in permeation of KT by 1.15, 3.93 & 5.5 fold respectively.
Furthermore, the combination of M and IPM dramatically increased the flux of KT to 855.32 ?g/cm²h, which was about 80.23 (P < 0.01) times comparable to that of control. The plasma concentration-time curves after topical administration fitted the two-compartment open model with first-order absorption. The mean values of AUC0-12 were 140.32, 48.1 & 266.0 ng hr/ml after IV administration and topical application of formula 4 and 8 respectively. The formulation containing IPM, M and ethanol showed the highest bioavailability (12.63 ±5.21) and it prolonged the duration of action (t½ is more than 7 hr) indicating a promising use in clinical situation.

4- Formulation and evaluation of novel mucoadhesive ketorolac tromethamine liquid suppository
Ketorolac tromethamine (KT) loaded mucoadhesive liquid suppository was prepared as a site-specific mucoadhesive rectal dosage form. Poloxamer mixture formed of 21% P407 and 9% P188 were used as liquid suppository base. In-vitro release rate of KT from liquid suppository was studied and compared to that from conventional suppository. The safety of the prepared suppository on GIT was conducted, hepatotoxicity of KT after 5 days of administration of liquid suppository was evaluated histologically and biochemically. The levels of liver enzymes alanine aminotransferase (ALT), aspartate amino transferase (AST), alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) were used as the biochemical markers of liver damage. The results obtained revealed that the addition of KT increased the gelation temperature of poloxamer gel and reduced the gel strength and the mucoadhesive force.

The study of the release rate of KT from liquid suppository was significantly higher than from conventional suppositories. Histological pictures of the GI tissues indicated no pathological damage after 5 days of rectal administration compared to oral administration. Also, it was revealed that no hepato-cellular damage occurred after administration of liquid suppository; unlike oral administration, which produced certain hepato-toxicity. The administration of KT liquid suppository did not significantly increase the basic levels of ALT and AST when compared to the control. On the other hand, the administration of KT oral solution in a dose of 10 mg/kg body weight/day for 5 days significantly increased serum ALT and AST levels, thus, KT liquid suppository in poloxamer gel was a convenient, safe and effective rectal dosage form for administration with lower hepato-
Caffeine Skin Delivery by Sonophoresis: In-vitro and In-vivo Evaluation from Different Gels

Abstract

The effect of ultrasound on caffeine transport through rabbit’s skin from four different gel matrices respectively made from- HPMC, methylcellulose, gelatin or carbopol 940 has been evaluated. The drug transport without ultrasound application was not detectable during the time course of the study. Ultrasound application has showed an increase drug transport (in terms of percent of drug transported, drug flux and permeability coefficient) with variable degrees according to the type of the applied gel. The order of % penetration was 25.6, 26.17, 32.72 and 65.02% w/v for, carbopol 940, gelatin, methyl cellulose and HPMC, respectively with corresponding increases in the values of flux and permeability coefficient in the same order. In vivo experiments were in agreement with the in vitro results. The amount of drug transported to the blood of living rabbits in term of peak concentration and AUC0-8 of the drug concentration plasma /time curves were significantly higher in the same order rank of the up mentioned gels. The viscosity was increased in the order of carbopol 940 < HPMC < gelatin < methylcellulose with respective values of 968.3, 1100.2, 2430 and 3352 m. Pa. Histological examination of rabbit skin has shown that no changes in the skin structure after ultrasound treatment at the same site twice daily for 3 consecutive days.

Comparative Bioavailability Study of Pipemidic Acid From Capsules and Suppositories

Abstract

Pipemidic acid suppositories were prepared using Witeplon His by fusion method, each containing 400 mg. For comparative study, hard gelatin capsules containing the same amount of the drug were prepared. A cross over bioavailability study of the prepared suppositories and capsules was performed using a group of 6 adult healthy human volunteers. It was found that, the cumulative amount of pipemidic acid excreted in urine within 24 h at each time intervals were higher in capsules. The drug excreted was calculated within 24 h in respect of the initial dose and found to be 20.5% and 13.75% from capsule and suppository respectively. Meanwhile, the time of maximum excretion rate was attained within 2.5 hour in both capsules and suppositories.

Preparation and Evaluation of Diclofenac Zinc and Bismuth Salts with Minimal Gastro-Intestinal Side Effects

Abstract

Both zinc and bismuth salts of diclofenac were prepared and characterized by IR and DSC. The pH-solubility profile at 25°C, in-vitro release patterns at 37°C by dissolution method and ulcerogenicity was determined for the prepared zinc and bismuth salts and compared with diclofenac sodium. The results revealed that, solubility of these salts was increased by pH elevation. The release of diclofenac zinc and bismuth salts showed a
sustained release profile, since about 50 and 55% of the drug was released after 6-hour dissolution from bismuth and zinc salt respectively. The prepared salts showed no hyperemia or gastric ulcer in animals which indicated that diclofenac salts with zinc or bismuth protects the stomach against gastric irritation and damage. Accordingly, this study is considered as a feasible approach in giving the drug with minimum side effects.

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EFFECT OF DRUG AND DRINK COMBINATION ON THE PH PROFILE OF SIMULATED GASTRIC JUICE

ABSTRACT
The pH profile of simulated gastric juice (SGJ) in presence of commercial antacids with and without frusemide (FR) and/or drink was studied. All the tested antacids elevated the pH of SGJ with different degrees. Both FR and drinks, each alone, markedly reduced the effect of some tested antacids.

9-

FORMULATION AND EVALUATION OF METRONIDAZOLE BIOADHESIVE MATRICES FOR TREATMENT OF PERIODONTITIS

Metronidazole (Mz) (an anaerobic antibacterial agent) was incorporated into different bioadhesive matrices including gels and films using carbopol 934p (4%), chitosan (3%) and hydroxypropyl methyl cellulose (HPMC) (3%). Penetration enhancers including menthol (1%) or oleic acid (OA) (5%, 10%) were incorporated in such formulations. The bioadhesive forces of the prepared matrices were determined and expressed as detachment stresses (Dyne/cm2). Permeability of Mz across ear rabbit skin and enhancement ratios (ER) were studied. The effects of selected Mz formulations on the healing rate of experimentally induced periodontitis in guinea pigs were estimated and histologically compared between treated and control groups. The obtained results showed that the gel formulations containing carbopol 934p exhibited maximum bioadhesive force with detachment stress equals to 66.98 X 10^2 dyne/cm2 followed by those containing chitosan (42.45 X 10^2 dyne/cm2) and HPMC (26.41 X 10^2 dyne/cm2). There was a statistically significant difference (P < 0.05) between the detachment stresses of gel formulations containing penetration enhancers and the corresponding ones without penetration enhancer. HPMC based films had bioadhesive force (19.33, 16 and 13.67 X 10^2 dyne/cm2) higher than those based on chitosan (5.33 and 7.33 X 10^2 dyne/cm2).

Also, it was noticed that the chitosan gel containing 1% menthol had the highest ER (5.13) among other gel formulations. On the other hand, chitosan based film containing 5% OA has the highest ER (1.73) among films. The effects of the selected formulations on the healing periodontal wound showed that bioadhesive chitosan gel containing menthol had accelerated the periodontal wound healing more than chitosan based film containing oleic acid.

10-

Formulation of Clindamycin Bioadhesive Gels for Localized Treatment of Periodontitis

Clindamycin hydrochloride (Clin HCl) gels were formulated using carbopol 934P (2, 3,
4%); chitosan (1, 2, 3%) and hydroxypropyl methyl cellulose (HPMC) (2, 3, 4%). Menthol and isopropyl myristate (IPM) (1, 3%) were added to the formulations as penetration enhancers. Bioadhesive forces of gel formulations were determined and expressed as detachment stresses (dyne/cm²). The permeabilities of drug from different gels through rabbit ear skin were investigated. The effects of the formulations on the healing of experimentally induced periodontitis on guinea pigs were evaluated histologically. The treatment started after induction of periodontitis in three groups and the remainder one acted as a control. At three different time points the animals of each group were sacrificed and mandibles specimens were extracted and prepared for subsequent histological evaluation. The periodontium healing parameters were compared between control and treated groups and histological pictures were captured. The results from gel formulations (4% carbopol), (3% HPMC) and (3% chitosan) were found to possess the highest detachment stresses 59.9, 37.3 and 43.4 (X102 dyne/cm²) respectively. However, the highest values of permeability were found to be 1.42, 6.7 and 2.83 (X10-2 gm/cm².hr) for formulations 4% carbopol with 1% IPM, 3% HPMC with 1% menthol and 3% chitosan with 1% menthol, respectively. The histological study revealed that the healing of the periodontium in treated groups was higher than control one. Meanwhile, the healing was as the following 3% chitosan with 1% menthol was higher than 4% carbopol with 1% IPM followed by 3% HPMC with 1% menthol.

**Formulation and characterization of ketotifen fumarate as niosomes in aerosol**

Niosomes, a novel vesicle entrapped with Ketotifen fumarate (KF), and delivered in aerosol has been prepared of span60 and cholesterol in molar ratios 3:1, 3:3, 3:5 were prepared by chloroform film method with sonication. Particle size, morphology of niosomes DSC, X-ray diffraction TEM, SEM, entrapment efficiency (EE%) and in-vitro release were estimated. The metered dose inhaler aerosol containing the selected niosomes ratio (3:3) was prepared by suspending niosomes equivalent to 20mg. KF in propellant H11 using soya lecithin as suspending agent. The valve is inserted and crimped into place to obtain canisters weight varies from 22.3-23.8 g. Additional propellant H12 is added to obtain the desired pressure using Pamasol packaging line. Aerosol was analyzed for leakage test, total number of puffs/container, weight/puff, delivered dose uniformity, and particle size of drug.

The results showed that niosomes were spherical in shape with particle size ranging between 2.3-5.7nm, KF was entrapped in not more than 73% w/w. KF release after 8h were 70%w/w, 65%w/w, 55%w/w for 3:1, 3:3, 3:5 respectively.

In addition, the leakage test was not more than 4mg/10 days, the number of puffs were not more than 200 puffs/can, the dose delivered per puff was 0.1 mg (20mg drug/can) and particle size ranges from 3.3-4.7nm.

These results are offering a novel approach to respiratory delivery of KF by aerosol.

**Formulation of Clindamycin Bioadhesive Gels for Localized Treatment of Periodontitis**

Clindamycin hydrochloride (Clin HCl) gels were formulated using carbopol 934P (2, 3, 4%); chitosan (1, 2, 3%) and hydroxypropyl methyl cellulose (HPMC) (2, 3, 4%). Menthol and isopropyl myristate (IPM) (1, 3%) were added to the formulations as penetration enhancers. Bioadhesive forces of gel formulations were determined and expressed as detachment stresses (dyne/cm²). The permeabilities of drug from different gels through rabbit ear skin were investigated. The effects of the formulations on the healing of experimentally induced periodontitis on guinea pigs were evaluated histologically. The treatment started after induction of periodontitis in three groups and the remainder one acted as a control. At three different time points the animals of each group were sacrificed and mandibles specimens were extracted and prepared for subsequent histological evaluation. The periodontium healing parameters were compared between control and treated groups and histological pictures were captured. The results from gel formulations (4% carbopol), (3% HPMC) and (3% chitosan) were found to possess the highest detachment stresses 59.9, 37.3 and 43.4 (X102 dyne/cm²) respectively. However, the highest values of permeability were found to be 1.42, 6.7 and 2.83 (X10-2 gm/cm².hr) for formulations 4% carbopol with 1% IPM, 3% HPMC with 1% menthol and 3% chitosan with 1% menthol, respectively. The histological study revealed that the healing of the periodontium in treated groups was higher than control one. Meanwhile, the healing was as the following 3% chitosan with 1% menthol was higher than 4% carbopol with 1% IPM followed by 3% HPMC with 1% menthol.
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