FORMULATION AND BIOAVAILABILITY OF DORZOLAMIDE AND PROPRANOLOL USING CYCLODEXTRINS IN TREATMENT OF GLAUCOMA

The influence of hydroxypropyl beta-cyclodextrin (HP-p-CyD) and beta-cyclodextrin (?-CyD) on the release characteristics and intraocular pressure of rabbits eyes using dorzolamide hydrochloride (Dorz) and propranolol hydrochloride (Prop) ocuserts was investigated. The two drugs are used individually as a new medical treatment for patients suffering from glaucoma in the form of topical carbonic anhydrase inhibitor (Dorz) and beta-blocker (Prop). The ocuserts were prepared using aqueous vehicles containing a mixture of sodium carboxymethyl cellulose and carbopol 941. The solid inclusion complexes of Dorz or Prop, were prepared by the kneading method in molar ratios of 1:1 (guest/host) with either HP-?-CyD or ?-CyD.

The released amounts of Dorz or Prop from ocuserts containing the drugs complexes with CyDs in (1:1) molar ratio were significantly higher than those from the formulations containing untreated drugs. The amounts released through cellophane membrane after six hours of Dorz were: 10.31, 14.41 and 20.71 mg from the ophthalmic ocuserts containing the untreated drug, drug-?-CyD complex and drug-HP-?-CyD complex, respectively. While, those of Prop were; 7.6, 11.5 and 18.7 mg from I the same formulations in the same arrangement.

The values of the maximum response (MR) of intraocular pressure (IOP) :release after the application of Dorz ocuserts containing drug alone, ?-CyD or HP-?-CyD complexes were; 14.9, 34.1 and 58.5 %. While, those of Prop ocuserts were;.43, 21.04 and 36.13%, respectively.

Also, the maximum response was higher in the case of drug-HP-?-CyD riplex than drug-?-CyD complex or the free drugs. The time of maximum response (MR) was achieved after 3 hr for both drugs in all formulations. In addition the values area under IOP-time curve (AUC) were; 57.25, 171.9 and 297.9 (%.hr) for Dorz. e. they were; 50.49, 111.97 and 198.13 (%.hr) for Prop, from the same brmulations in the same arrangement.

CONTROLLED RELEASE TABLETS FOR CAPTOPRIL

The purpose of this investigation was to prepare and study the drug release behavior from tablet matrices containing captopril. Four types of polymers in different concentrations, namely; guar gum (a non-ionic polysaccharide), three different grades of carbomers (floating, bioadhesive polymers; carbopol 971, carbopol 980 and carbopol 934), were utilized to prepare the tablets. Different formulations containing the selected polymers (individually) and other tablet excipients (lactose, avicelâ€™ or emcompress) were compressed into tablets utilizing a single punch tablet machine. The Physical properties and release characteristics of the prepared tablets were investigated.

All tablets were found to comply the pharmacopeia! limits as regards the physical properties. Meanwhile, the formulations containing guar gum exhibit lower hardness values when compared with those containing carbomers. The former have a higher friability than the latter. All tablets containing guar gum or carbomer exhibited sustained release behavior for captopril. The release data were subjected to Anova, single factor test. It was found that, there was no significant difference between the formulations.
containing the same polymer. Also, neither the concentration of the polymer nor the co-
excipient has a significant effect on the release behavior of the drug from the tablets. All
the prepared tablets containing polymers follow Higuchi model via Fickian diffusion
mechanism and therefore, they could be used as promising systems for preparing
captopril controlled release tablets.

3-

**EFFECT OF ATROPINE SULFATE OINTMENTS AND GELS ON THE
INTRAOCULAR PRESSURE OF RABBITâ€™S EYE**

Atropine sulfate has been formulated in ointments and gels using absorption base,
hydrocarbon base, water soluble base, polyvinylpyrrolidone gel and sodium
carboxymethylcellulose gel. The release behaviour of the drug and the effect on
intraocular pressure of rabbitâ€™s eye have been estimated. The results revealed that, the
release of atropine sulfate was in the following order, polyvinylpyrrolidone gel >
polyethylene glycol > sodium carboxymethylcellulose gel > lanolin-petrolatum >
hydrocarbon base. However the maximum effect of drug on intraocular pressure was
maintained within three hours in the following order, sodium carboxymethylcellulose gel <
hydrocarbon base < polyethylene glycol base < polyvinylpyrrolidone gel <; lanolin
-petrolatum base.

4-

**EFFECT OF VEHICLE COMPOSITION ON BIOAVAILABILITY OF
ATROPINE SULFATE IN RABBITS EYES**

The effect of vehicle composition on ocular disposition
of atropine sulfate was studied using different ophthalmic
drops, ointments and gels on rabbitâ€™s eyes. The
bioavailability of the drug in eye tissues showed that, their
distribution were greatly affected by the type of the
vehicle. In addition, the uptake by different eye tissues
was variable. The peak time of atropine sulfate
was found to be 2 hours for ophthalmic drops and 3 hours in case of ointments and gels.
The total bioavailability of atropine sulfate in eye tissues of rabbit and aqueous humor
after 2 hours were 4350, 4010 and 3675 ug/mgm using â€œCMC, PVP and PEG
ophthalmic drops. While that from ointments and gelr. after 3 hours were 4 355, 4
320,4255 and <205 ug/mgm for PVP gel, PEG base, hydrocarbon base and NaCHC gel
respectively.

5-

**FORMULATION AND STABILITY OF ATROPINE SULFATE EYE DROPS**

Atropine sulfate was formulated in ophthalmic solutions using Methyl cellulose, Sodium
carboxymethyicellulose, polyvinyl alcohol, polyethylene glycol 6000 and polyvinyl-
pyrro-lidone K7r. The formulations were subjected to stability studies. The obtained
results revealed that, no degradation or complexation occur among the tested
preparations with the exception of that contained methylcellulose. A significant
increase of drug content and viscosity of the solution was beginning after storage for the
first month. Furthermore, the degradation in drug concentration was reached more than
10% after storage at 70 C for two years. Also TLC revealed a chemical decomposition of
atropine sulfate in methylcellulose?ol

6- Formulation and evaluation of a buccoadhesive captopril tablets

Buccoadhesive tablets of captopril were prepared by direct compression of the drug with different polymers; Carbopol 934 (CP 934), Eudragit RS 100 (EU RS 100), Chitosan (Ch), Hydroxypropyl methylcellulose (HPMC) and Polyvinylpyrrolidone K30 (PVP K30) either singly or in blends of different ratios. The tablets were evaluated for their weight variation, drug content uniformity, friability, hardness, swelling index, surface pH, in-vitro bioadhesive strength and release characteristics. The bioavailability and the pharmacokinetics parameters of captopril from two selected formulations (CP 934:HPMC 6:4 and Ch:HPMC 6:4) were evaluated.

The in-vitro bioadhesive strength and release characteristics were found to be a function of the type of polymer, ratio of polymer blends. Swelling and bioadhesive characteristics were determined for both plain and medicated tablets. The high concentration of carbopol and chitosan containing formulations showed the greatest adhesive strength. The mean pharmacokinetic parameters of captopril after buccoadhesive tablet administration were: Cmax 506.9 ng/ml, Tmax 4 hr, AUC0-8 2359.5 ng.hr/ml for CP 934: HPMC (6:4), while Cmax 429.02 ng/ml, Tmax 2.67 hr, AUC0-8 1637.43 ng.hr/ml for Chitosan: HPMC (6:4). In comparison, in case of oral administration of control tablet the Cmax 591.28 ng/ml, Tmax 1.5 hr, AUC0-8 1869.29 ng.hr/ml.

7- Stability of Enrofloxacin-Cyclodextrin Complexes and Healing Time of Inflamed Rabbits Eyes

The inclusion complexes of enrofloxacin with cyclodextrins (CyDs); hydroxypropyl beta-cyclodextrin (HP-?-CyD) and beta-cyclodextrin (?-CyD) were prepared in molar ratio (1:2). The ophthalmic gels [sodium carboxymethyl cellulose (sod. CMC), sodium alginate] and ointments [emulsion, absorption and water soluble bases (W.S.B)] were prepared using 0.5% of the drug or equivalent amounts of its complexes with HP-?-CyD or ?-CYD.

The formulations were subjected to stability study at different temperatures (25, 35 and 45 °C). It was of interest to study the effects of enrofloxacin ophthalmic ointments and gels on the inflamed rabbits eyes. Also, to study the effect of the vehicle on the rate of healing as well as physiological changes in rabbit eyes treated with these formulations. The obtained results revealed that, these formulations exhibited the best physical and chemical stability up to 6 months of storage at 25, 35 and 45°C. The complexation of the drug with HP-?-CyD proved to be superior in stability when incorporated in W.S.B and sod. alginate gel and these complexes showed best stability than that with ?-CyD followed by the drug alone. After the clinical healing of ulcers in inflamed rabbits eyes, the denuded layers were completely regenerated and the photomicrographs showed nearly normal eye tissues.

8- Ocular Bioavailability of Enrofloxacin-Cyclodextrin Complexes from certain Ophthalmic Preparations in Rabbits Eyes

The effect of inclusion complexes of enrofloxacin (Enr) with cyclodextrins (CyDs);
hydroxypropyl beta-cyclodextrin (HP-?-CyD) and beta-cyclodextrin (?-CyD) was studied. These complexes were prepared in a molar ratio (1:2). The ophthalmic gels [sodium carboxymethyl cellulose (sod. CMC), sodium alginate] and ointments (emulsion, absorption and water soluble bases) were prepared using 0.5% of the drug or equivalent amounts of its complexes with HP-?-CyD or ?-CyD. The ocular disposition of the drug in rabbitâ€™s eyes has been studied.

The obtained results revealed that, all tested formulations provided the highest Cmax of the drug in conjunctiva followed by cornea, iris-ciliary body, and then aqueous humor. The peak time of maximum drug concentration in rabbitâ€™s eye tissues and aqueous humor was two hours for various ophthalmic ointments and gels. The total availability of enrofloxacin was improved when the drug was complexed with HP-b-CyD.

9-

Efficacy of Topical Ketoconazole Cyclodextrins Complexes in Treatment of Oral Candidiasis

Background. A new formulation for topical administration of ketoconazole (KET) in the oral cavity has been developed using sodium carboxymethyl cellulose (sod. CMC) as mucoadhesive polymer. The drug was prepared in different formulations (buccal patches and gels). Theses formulations were used for the treatment of oral candidiasis in immuno suppressed patients. Methods. The drug complexes were prepared by the kneading method. Either buccal patches or gels of sodium carboxymethyl cellulose were containing 2 % ketoconazole, 2 % KET-?-CyD complex and 2 % KET HP-?-CyD complex. The influence of cyclodextrins (CyDs); hydroxypropyl beta -cyclodextrin (HP-?-CyD) and beta-cyclodextrin (?-CyD) on the aqueous solubility and release characteristics of ketoconazole (KET) from the buccal patches and gels were investigated. Thirty six immunosuppressed patients with oral candidiasis were divided into 6 groups; each group (containing four females and two males) was treated topically with a special formula of the drug. The efficacy was evaluated on a base of clinical response and mycological study. Results. X-ray diffractometry (XRDP) and differential scanning calorimetry (DSC) revealed that, the aqueous solubility of KET was significantly increased by the formation of (1:1) inclusion complexes with CyDs. However, the solubility of KET was increased linearly as a function of HP-?-CyD followed by ?-CyD. Moreover, at all time intervals, the amounts of the drug released from buccal patches or gels containing either the drug alone or its complexes with CyDs were significantly higher in case of HP-?-CyD followed by ?-CyD then the drug alone. From the kinetic estimation of the release data, it was evident from the results that, the best fitting line with the highest correlation coefficient (r) was found for first-order kinetics for buccal patches and gels containing drug alone or drug-HP-?-CyD complexes. While, in case of buccal patches and gels containing drug-?-CyD complexes, the best fitting line with the highest correlation coefficient was found with Higuchi model. In the clinical studies the response of the disease to all formulas was excellent with significantly higher percentage of response in group V 98.8% and VI 97.5% (patches and gels containing KET-HP-B CYD respectively) with shortest duration of treatment 7 ± 2 and 9 ± 2.8 days respectively than other formula. The direct microscope examination and culture for candida albicans were positive in all patients before treatment. After treatment, presence of hypae and budding cells occurred in only 5.6%of patients by direct microscopic examinations and +ve culture for candida albicans was present in only 22.2 % of patients. Conclusion. The
mucoadhesive formulations offer many advantages in the treatments of oral candidiasis and can be proposed as a new therapeutic tool against buccal diseases. The best formulation is the patch and gel containing KET-HP-B CD.

10-

Bioavailability and Ocular Disposition of Ketorolac Tromethamine from Various Ophthalmic Preparations

Most formulations (including eye drops) could be stored for 6 months at 25oC, 35oC, 45oC without physical or chemical degradations of the drug. However, PVA and absorption bases showed some changes in the drug content (t90 was 2.84 months for both at 45oC). The decomposition rate of ketorolac tromethamine followed the first-order degradation kinetic. The highest stable formulae are, sod CMC eye drops and gel (t90 values were, 151.9 and 91.18 months, respectively at 45oC). The highest concentration of the drug (Cmax) from all tested formulations is provided in conjunctiva followed by cornea, iris-ciliary body, then aqueous humor. The peak time for maximum drug concentration (T max) from sod CMC eye drops was two hours. While, that for sod CMC gel, PVA ointment and gelatin ocuserts was three hours in all tissues after the application of the tested formulations. In addition, the total availability of the drug from the tested formulations was in the following order: gelatin ocuserts > sod CMC gel > PVA ointment > sod. CMC eye drops.

11-

Formulation and In-Vivo Evaluation of Ketotifen Fumarate Ophthalmic Preparations in Rabbits eyes

Ketotifen fumarate was incorporated in some ocular formulations including eye drops, gels using sodium carboxymethyl cellulose (sod CMC), polyvinyl pyrrolidone k30 (PVP K30) and ophthalmic ointments employing fatty base, absorption base, Polyethylene glycol base, and polyvinyl alcohol base (PVA). In addition, the release characteristics and stability of ketotifen fumarate from these ophthalmic preparations were investigated. Furthermore, the effect of the drug on the non-infectious red eye conjunctivitis was studied.

The obtained results revealed that, ketotifen fumarate could be formulated in these bases. The amounts of drug released from sod CMC eye drops and gels were higher than that released from PVP K30 eye drops and gels. It was found that, the type of the ointment base could affect greatly the amount of the drug released and could be arranged in the following order, PVA ointment > water soluble ointment > absorption base ointment > fatty base ointment.

Such formulations could be stored for 6 months at 25oC, 35oC and 45oC without physical or chemical degradations of the drug formulations, except the ointment containing fatty base which showed significant changes in the drug content. The average decongestion times of the inflamed rabbits eyes treated with the selected formulations are significantly influenced by the type of the drug carriers used. Normal conjunctiva and cornea with no mucus discharge were observed after treatment. They can be arranged in the following order; PVA ointment > sod CMC eye drops > sod CMC gel.

12-

The Effect of Binder Type and Major diluent on the Migration and Bioavailability of Riboflavin Sodium Phosphate during Tablet Making
The migration of riboflavin sodium phosphate (RSP) upon drying of its wet granules was studied through the formulation of granules using different diluents (lactose monohydrate and anhydrous dibasic calcium phosphate), different binders of different concentrations; polyvinyl pyrrolidone (PVP k25), methylcellulose (MC), hydroxypropylmethyl cellulose (HPMC) and gelatin at different drying temperatures (50° C and 70° C). The prepared granules were compressed into tablets and evaluated. In vitro drug release from the formulated tablets was performed. In addition, in vivo study was conducted on some selected tablet batches.

The results showed that, the granules prepared with dibasic calcium phosphate showed lower migration for the drug than those prepared with lactose. Also, drug migration decreased with increasing the binder concentration and viscosity. The degree of tablet mottling was inversely proportional to the binder concentration. Tablets prepared with 10 % w/w gelatin were found to be the least mottled ones. In addition, they showed the least friability percentage, the highest hardness value and the highest disintegration time. Tablets prepared with 0.5 % MC showed the highest dissolution rate, however, those prepared with 10 % gelatin had the lowest dissolution rate. Generally, increasing the binder concentration resulted in slowing the in vitro drug release from tablets.

The in vivo study showed that, tablets prepared with 10 % w/w gelatin showed the lowest excretion rate and the highest Tmax (1.5 hours). Meanwhile, tablets prepared using 0.5 % w/w MC exhibited higher excretion rate and Tmax of 0.5 hour.

13-

Potential Use of 2-Hydroxypropyl-b-cyclodextrin for Preparation of Orally Disintegrating Tablets Containing dl- a-Tocopheryl Acetate, an Oily Drug

To expand the application of a drug in orally disintegrating tablets, the potential use of b -cyclodextrin (b - CyD) and 2-hydroxypropyl-b -cyclodextrin (HP-b -CyD) as excipients for the tablets containing dl-a-tocopheryl acetate (VE), an oily drug, was evaluated. HP-b -CyD, not b -CyD, solubilized VE in water through the formation of higher order of complexes at the molar ratio of 1 : 2 (VE : HP-b -CyD). When prepared under the optimal preparation conditions, the VE tablets containing lactose and 5% (w/w) of HP-b -CyD, not b -CyD, had high hardness more than 4 kg and rapid disintegration within 100 s both in vitro and in vivo. In addition, VE tablets containing lactose and 5% (w/w) of HP-b -CyD, not b -CyD, maintained the high hardness and rapid disintegration under the accelerated stability test using different conditions for 4 weeks. Therefore, these results suggest the potential use of HP-b -CyD, not b -CyD, as an excipient for orally disintegrating tablets containing VE, an oily drug, in the molding method.

14-

FORMULATION AND STABILITY STUDY OF NAPROXEN OPHTHALMIC
PREPARATIONS

Naproxen was formulated in different ophthalmic preparations as drops, gels and ocuserts using cellulose derivatives such as methylcellulose, sodium carboxymethylcellulose and hydroxypropyl methylcellulose. All the prepared formulae (drops, gels and ocuserts) containing the drug were subjected to the study of the release characteristics. Also, the stability of naproxen ophthalmic preparations at different conditions of storage were investigated. The obtained results revealed that, the percentage released of naproxen from the three ophthalmic dosage forms after 7 hours were found to be in the following order; Drops > ocuserts > gels. These formulations exhibited the highest physical and chemical stability up to 6 months of storage at 25°C, 35°C and 45°C, except the formulae containing methylcellulose polymer, showed the least stable formulations. The drug content in the formulae containing methylcellulose was decreased about 10% after storage at different temperatures for 6 months.

STABILITY OF ENROFLOXACIN-CYCLODEXTRINES COMPLEXES AND HEALING TIME OF INFLAMED RABBITS EYES

The inclusion complexes of enrofloxacin with cyclodextrins (CyDs); hydroxypropyl beta-cyclodextrin (HP-?-CyD) and beta-cyclodextrin (?-CyD) were prepared in molar ratio (1:2). The ophthalmic gels [sodium carboxymethyl cellulose (sod. CMC), sodium alginate] and ointments [emulsion, absorption and water soluble bases (W.S.B)] were prepared using 0.5% of the drug or equivalent amounts of its complexes with HP-?-CyD or ?.CyD. The formulations were subjected to stability study at different temperatures (25, 35 and 45°C). It was of interest to study the effects of enrofloxacin ophthalmic ointments and gels on the inflamed rabbits eyes. Also, to study the effect of the vehicle on the rate of healing as well as physiological changes in rabbit eyes treated with these formulations. The obtained results revealed that, these formulations exhibited the best physical and chemical stability up to 6 months of storage at 25, 35 and 45°C. The complexation of the drug with HP-?-CyD proved to be superior in stability when incorporated in W.S.B and sod. alginate gel and these complexes showed best stability than that with ?-CyD followed by the drug alone. After the clinical healing of ulcers in inflamed rabbits eyes, the denuded layers were completely regenerated and the photomicrographs showed nearly normal eye tissues.

In-Vitro Evaluation of Enrofloxacin Ophthalmic Preparations Containing Cyclodextrins

The effect of cyclodextrins (CyDs); hydroxypropyl beta-cyclodextrin (HP-P-CyD) and beta-cyclodextrin (P-CyD) on the solubility and release characteristics of enrofloxacin (Em) from ophthalmic ointments and gels were investigated. The ophthalmic gels (sodium carboxymethyl cellulose, sod. CMC) and sodium alginate) and ointments (emulsion, absorption and water soluble bases) were prepared using 0.5% of the drug or equivalent amounts of its complexes with HP-P-CyD or P-CyD. The results revealed that, the aqueous solubility of enrofloxacin was significantly increased by the formation of (1:2) inclusion complexes with CyDs. However, the solubility of enrofloxacin was increased linearly as a function of HP-P-CyD followed by P-CyD. The amounts of the drug released from the prepared formulations were ananged in the order of; water soluble
Moreover, at all time intervals, the amounts of the drug released from ophthalmic gels and ointments containing either the drug alone or its complexes with CyDs in molar ratio (1:2) were significantly higher in case of HP-P-CyD followed by P-CyD then the drug alone.

**Effect of the Base Type and Volatile Oils on the Transdermal Delivery Characteristics of Captopril**

In this study, different topical formulations using oleaginous, emulsion and water soluble bases containing 1 % (w/w) captopril were prepared by the fusion method. The penetration behavior of captopril from these preparations was studied through excised rabbit skin. The influence of the base type as well as some of the volatile oils on the mechanism and transdermal delivery characteristics of the drug was investigated. At the end of experiments, the percentage of the drug transported was 89.66, 83.18 and 63.87 from emulsion, oleaginous and water soluble bases, respectively. The addition of volatile oils to the oleaginous base delayed the transport of the drug in the following order of magnitude: thymol < menthol < methyl salicylate < cinnamaldehyde < camphor. This inhibition was significant (P<0.05) in case of alcoholic (menthol) and phenolic (thymol) monoterpenes, whereas other oils exhibited no significant effect. The Ex-v/vo drug penetration from the tested formulations through excised rabbit skin appeared to occur according to both Higuchi and Fickian models. The obtained results could be utilized as a guide on the way to formulate captopril transdermal drug delivery systems (TDDS).

**pH-independent Controlled Release Tablets Comprising Weakly Acidic Drug: Design and Evaluation**

The release of weakly acidic drugs is dependent on the environmental pH in the GIT fluid. These drugs are not capable to be released or dissolved in the acidic media with pH lower than their pKa values, hence, reduce their absorption from this specified site of the GIT. Preparation of pH-independent controlled release of such drugs was therefore adequate. Tablets were prepared by compressing mixtures of indomethacin (model drug), PVP, and tromethamine (as an alkalinizer) in order to attain independent release pattern. The tablets were coated with 5% ethyl cellulose in ethyl acetate on the lateral site leaving two surfaces free or coated at all surfaces except one. When the composition of tromethamine to the drug in the mixture was equal to or more than 4.5 : 1, the tablets showed pH-independent release. Release rate was controlled with tromethamine/drug ratio, the percent and type of PVP and the surface area available for drug release. Release rate can be altered freely while maintaining the pH-independent release characteristics by combining the different composition matrices. Analysis of the dissolution data revealed that mixed zero-order and higuchi linear square root of time relationships with lag time was the best model to describe indomethacin release kinetics.

**Formulation and Preparation of Ketoprofen Tablets Using Interpolymer Complexes Techniques**

The application of interpolymer complexes (IPCs) for oral controlled drug delivery
systems was tried between Eudragit E 100 and various anionic polymers viz. sodium alginate, sodium carboxymethylcellulose and pectin. The prepared interpolymer complexes were investigated using Fourier transform infra-red spectroscopy and differential scanning calorimetry. The stoichiometric ratios of Eudragit E with the anionic polymers were determined by measuring the viscosity at different pH values. Ketoprofen tablets were prepared using polymers alone, physical mixtures of Eudragit E with sodium alginate, sodium CMC or pectin in different ratios 1:3, 1:1 and 3:1, and the corresponding interpolymer complexes of these polymers. Evaluation of the prepared tablets including weight variation, thickness, content uniformity, friability percent, and in-vitro release studies using 0.1 N HCl and phosphate buffer of pH 7.4 as dissolution medium were performed. The tablets showed an acceptable physical properties and the dissolution rate data were found to be dependent on the type of IPC, the physical mixture of Eud. E and each of the anionic polymers and also on the pH of the dissolution medium. Eudragit E - sod. CMC physical mixture 1:1 and Eud. E - sod. CMC IPC were selected for the in-vivo study in rabbits. The results showed a lower peak plasma concentration and marked sustained release effect compared to the control tablets.

20-

**Comparative Bioavailability Study of Pipemidic Acid From Capsules and Suppositories**

Abstract

Pipemidic acid suppositories were prepared using Witepsole 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. Mean while, the time of maximum excretion rate was attained within 2.5 hour in both capsules and suppositories.

21-

**Ocular Bioavailability of Triamcinolone Acetonide Complex from Different Ophthalmic Preparations in Rabbits’ Eyes**

Objectives: The effect of beta-cyclodextrin (β-CyD) on the solubility, release characteristics and ocular bioavailability of triamcinolone acetonide (TA) from ophthalmic gels and ocluserts were investigated.

Methods: Triamcinolone acetonide-β-CyD complex was prepared by kneading method in a molar ratio of 1:1. The ophthalmic gels [carbopol 934, hydroxy propyl methyl cellulose (HPMC), sodium alginate] and ocluserts (HPMC and carbopol 934 combination, sodium alginate and carbopol 934 combination) were prepared using 0.1% of the drug or its equivalent amount of complex with 2-β-CyD. The in vivo study was performed on male albino rabbits. The drug concentrations were determined in different eye tissues and aqueous humor of the rabbits after 1, 2, 4, and 6 hr of the application by HPLC method.
Results: The obtained results revealed that, the solubility of TA was increased linearly as a function of $\gamma$-CyD concentration following AL type phase solubility diagram. The percent released of the drug from the prepared formulations containing TA untreated could be arranged in the following order; HPMC and carbopol 934 combination ocuserts > sod. alginate and carbopol 934 combination ocuserts > HPMC gel > carbopol 934 gel > sod. alginate gel. Moreover, at all time intervals, the percent released of the drug from ophthalmic gels and ocuserts containing the drug complex with $\gamma$-CyD was significantly higher than that of the untreated drug. Concerning the ocular bioavailability, all tested formulations provided the highest Cmax of the drug in conjunctiva followed by cornea, iris-ciliary body, then the aqueous humor, except that after 6 hr, it was high in cornea followed by iris-ciliary body, conjunctiva and then the aqueous humor. The peak time of maximum drug concentration (Tmax) in rabbits' eye tissues and aqueous humor was 4 hr for all ophthalmic gels and ocuserts.

Conclusions: The total ocular bioavailability of triamcinolone acetonide was improved when the drug was complexed with b-CyD.