International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 4(2): March-April 2014

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences **Original Article……!!!**

Received: 11-01-2014; Revised; Accepted: 20-04-2014

NEW TOPICAL DELIVERY OF LIDOCAINE HCL

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Keywords:

Lidocaine HCl, anti-arrhythmic drug, pediatric venipuncture, neuropathic conditions, transdermal delivery

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ABSTRACT

Lidocaine HCl is a local anesthetic widely used for a variety of medical procedures like treatment of open skin sores, lesions, and surgical procedures such as suturing of wounds and venipuncture[17]. Lidocaine is used in various dental procedures. It is also a first line anti-arrhythmic drug when administered to the heart in large doses. The most common method of lidocaine delivery is through intravenous or hypodermic injections. When Lidocaine is injected as analgesic agent; the discomfort caused by the application is counterproductive to the pain-relieving effect of the drug[7]. For purposes such as preparation for pediatric venipuncture, in relieving pain associated with neuropathic conditions (for eg. diabetic neuropathy, postherpetic neuralgia, soft tissue rheumatism), a painless means to administer Lidocaine would be an important procedure[5]. Moreover, since it has a short half-life after parenteral administration, an alternate route to achieve the substantially sustained analgesic effects while avoiding any side effects needs to be considered. Of the many drug delivery systems, the percutaneous drug delivery system is one of the most widely used. This makes local transdermal delivery of Lidocaine a favourable avenue of research.

INTRODUCTION

Lidocaine HCl is a local anesthetic widely used for a variety of medical procedures like treatment of open skin sores, lesions, and surgical procedures such as suturing of wounds and venipuncture[17]. Lidocaine is used in various dental procedures. It is also a first line anti-arrhythmic drug when administered to the heart in large doses. The most common method of lidocaine delivery is through intravenous or hypodermic injections. When Lidocaine is injected as analgesic agent; the discomfort caused by the application is counterproductive to the pain-relieving effect of the drug[7]. For purposes such as preparation for pediatric venipuncture, in relieving pain associated with neuropathic conditions (for eg. diabetic neuropathy, postherpetic neuralgia, soft tissue rheumatism), a painless means to administer Lidocaine would be an important procedure[5]. Moreover, since it has a short half-life after parenteral administration, an alternate route to achieve the substantially sustained analgesic effects while avoiding any side effects needs to be considered. Of the many drug delivery systems, the percutaneous drug delivery system is one of the most widely used. This makes local transdermal delivery of Lidocaine a favourable avenue of research.

ADVANTAGES

Transdermal delivery of drug offers the following advantages over other routes of delivery[27].

- ❖ Avoidance of the risk and inconveniences of intravenous therapy and of the varied conditions of absorption, pH changes, presence of enzymes, gastric emptying time, etc.
- ❖ Continuity of administration, permitting the use of a drug with a short biological half-life.
- ❖ Achievements of efficacy with lower total daily dosage of drug by continuous drug input and bypassing hepatic first –pass metabolism.
- ❖ Less chances of over- or under-dosing as a result of prolonged pre-programmed delivery of drug at the required therapeutic dose rate.
- ❖ Better patient compliance.
- ❖ Ability to easily terminate the medications, when needed, if any toxicity appears.
- ❖ Ability to modify the properties of the biological barrier to absorption.
- ❖ A relatively large area of application in comparison to nasal and buccal cavity.

► **Formulation of Lidocaine HCl gel $F_1 – F_5$:-**

Procedure:- Lidocaine HCl was dissolved in a solvent mixture of ethanol, propylene glycol and water. It was stirred manually so that the drug dissolves. The specified quantity of carbopol 940 was sprinkled in the above mixture and was simultaneously stirred to disperse it. The dispersion was allowed to stand for 1 day so that carbopol gets soaked and swelled.

The solution was then subjected to agitation by mechanical stirrer at 600 rpm to get a smooth dispersion. Then the dispersion was allowed to stand so that any entrained air could escape. To this prepared dispersion triethanolamine was added drop by drop and stirred to get a smooth gel.Ethanol and Propylene glycol added in gel also served as preservative so no other preservatives were added.

Contents	Formulation				
	F_1	F_2	F_3	F_4	F_5
Lidocaine HCl %	2	2	2	2	2
Carbopol 940 %	1	1	1	1	1
Triethanolamine %	0.5	0.5	0.5	0.5	0.5
Propylene glycol %	10	15	20	25	30
Ethanol %	10	10	10	10	10
Water % (up to 100 %)	q.s.	q.s.	q.s.	q.s.	q.s.

►EVALUATION

Procedure

The developed formulations were subjected to *in vitro* diffusion study through dialysis membrane (HIMEDIA) with molecular weight cut off 12000-14000 KD using modified Keishary Chien cell. Accurately weighed quantity was placed on the membrane separating donar compartment from receptor compartment. The donar compartment was covered with aluminium foil to avoid atmospheric influence. The receptor compartment was filled with saline phosphate buffer pH 7.4. The whole assembly was maintained at 37±1˚C and the receptor solution was stirred with magnetic stirrer at 600 rpm throughout the experiment. Care was taken that no air bubbles were trapped under the membrane. Aliquots of 1ml were with drawn at regular intervals of 1hr for a period of 8hr and replaced with equal volume of fresh medium equilibrated at 37±1˚C. All samples were diluted to 10 ml medium and analysed for Lidocaine HCl content spectrophotometrically at wavelength 262.8nm.

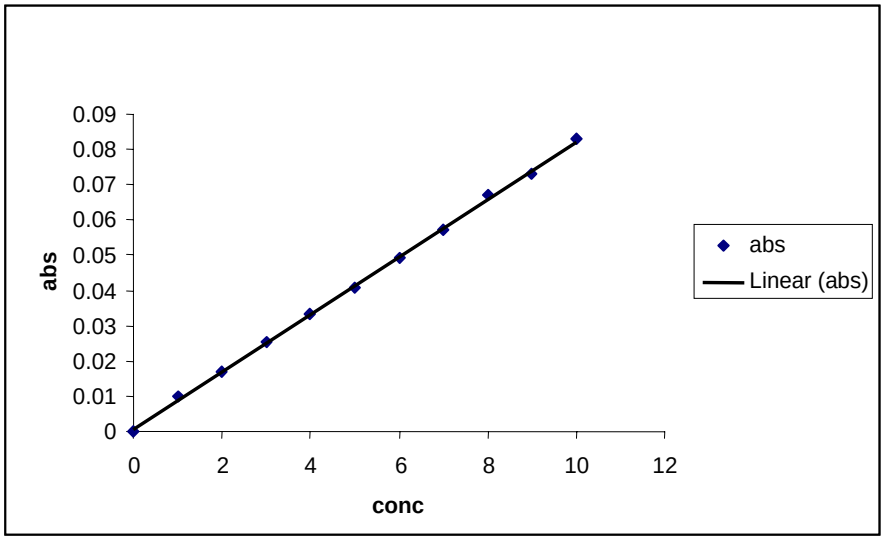
a. Color, odour, appearance and feel:

S.No	Parameter	Gels		
		F_{Pg}	F_{Eg}	$F_{Pg/Eg}$
1	Color	Colorless transparent	yellow	Cream
2	Clogging	-	-	-
3	Odour	Pleasant	pleasant	Pleasant
4	Feel	Smooth	smooth	smooth

a. Drug content and uniformity:

Standard caliberation curve :

S.No	Conc in (µg)	Absorbance
1	0	0
2	1	0.012
3	2	0.017
4	3	0.028
5	4	0.035



b. pH:

S.No	Formulation	pH*
1	F_1	6.13
2	F_2	6.27
3	F_3	6.50
4	F_4	6.42
5	F_5	6.35

a. Spreadability:

S.No	Formulation	1	2	3	Spreadability (gm.cm/sec)*
1	F_1	21.87	22.6	21.18	21.88±0.71
2	F_2	22.6	23.37	22.6	22.85±0.45
3	F_3	21.18	20.05	22.6	21.43±1.07
4	F_4	24.21	24.42	23.37	23.91±0.52

a. Viscosity

S.No	Formulation	Viscosity (cp)
1	F_1	84700
2	F_2	82400
3	F_3	92800
4	F_4	78400
5	F_5	73600

DISCUSSION AND CONCLUSION

The Lidocaine HCl used throughout the study was of pure quality. The gelling agent cabopol 940 was also subjected to confirmatory identification testing. The identification tests were conducted as per official tests under U.S.P 2000. Carbopol 940 showed compliance with official specification. Different formulations of Lidocaine HCl gel containing Propylene glycol and Eugenol and their mixture as penetration enhancers with gelling agent cabopol 940 in hydroalcholic solutions were prepared. Since Lidocaine HCl has very poor penetration through the intact skin, penetration enhancers were incorporated. Propylene glycol and Eugenol were used as primary penetration enhancers. Ethanol provided elasticity to the gels and also acted as a secondary penetration enhancer. All the formulations were evaluated for their appearance, feel, drug content and content uniformity, pH, viscosity, spreadability, *in vitro* diffusion study through dialysis membrane, and *in vitro* permeation study through rat abdominal skin.

Flyn and Gordon[39] have stated that the appearance, feel, drug content and content uniformity, and pH of semisolid preparations are the measure of evaluating physical and chemical stability of gels and other semisolids. Stress was also given to pharmaceutical elegance in discussion. These included the ease of application, feel of the preparation once it is on the skin, and the appearance of the applied film. Lidocaine HCl also showed a maximum release at 25% propylene glycol, so here also it can be concluded that on further increasing the concentration of PG, the decrease in drug release was due to the reduced partitioning of the drug from the vehicle to the skin as Lidocaine HCl and Tenoxicam have the same partition coefficient: Log *P* (octanol/water)

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