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FORMULATION AND EVALUATION OF METFORMINE HYDROCHLORIDE GEL FOR WOUND HEALING

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Abstract :

Diabetes mellitus is the metabolic disorder that obstruct the normal step of wound healing.Metformin hydrochloride having anticoagulant, anti-inflammatory and anti proliferative effect that could affect wound healing or risk of wound complication after surgery or injury. The objective of the present study was to develop formulation of metformin hydrochloride in different gel including hydroalcoholic ,hydrogel ,microemulsion, anhydrous gel and alcoholic gel bases. The result shows that all gel formulation showed good and acceptable physical properties. The obtained data from release study revealed that the total amount of drug release was affected the nature ofthe basewith maximum drug release wasalcoholic>hydrogel >hydroalcoholic>anhydrous >microemulsion gel base. Statistical analysis resulting that the higher release rate of the first three gel bases was significant when it compare to the anhydrous and microemulsion gel bases.The result of the different chemical and physical test of metformin hcl gel showed that the formation could be used topically in order to protect skin damage and these formulation for better absorption and penetration of the active moiety into the systemic circulation. In this different gelling agent can be used to formulate topical gel of metformin hydrochloride for long term stability study as per ich guidelines.

Keywords : Xanthum gum, Guar gum, Metformin HCL-gels -Drug Release-Wound Healing

INTRODUCTION: -

TOPICAL DRUG DELIVERY: -

Topical drug delivery system serveas one of the most easily accessible routes for drug administration. Topical delivery is defined as the application of pharmaceutical dosage form to the skin treatment of cutaneous disorder or the cutaneous manifestation of the general disease with the intent of confining the pharmacological or other effect of the drug to the surface of the skin(1). Topical delivery is an attractive route for local and systemic treatment. The delivery of drugs onto the skin is recognized as an effective means of therapy for local dermatologic diseases. It can penetrate deeper into skin and hence give better absorption. Topical application has many advantages over the conventional dosage forms. In general, they are deemed more effective less toxic than conventional formulations due to the bilayer composition and structure.

In the formulation of topical dosage forms, attempts are being made to utilize drug carriers that ensure adequate localization or penetration of the drug within or through the skin in order to enhance the local and minimize the systemic effects to ensure adequate percutaneous absorption Topical preparation avoids the GI-irritation, prevent the metabolism of drug in the liver and increase thebioavailability of the drug. Topical preparations give its action directly at the site of action(1,2).

Skin covers the large surface of body combines with the mucosal lining of the respiratory, digestive, urinogenital tract toform capsule which separate internal body structure from the external environment. The average area of the skin about 2 square and ph of thwe skin varies from 4 - 5.6 . Skin consisting three layers outermost layer is called epidermis middle layer is the dermis and inner one is hypodermis. wound healing is the process of the restoring the normal structure of damaged tissue. The process involves hemostasis ,inflammation, proliferation and remodelingregeneration(3)

Metformin hydrochloride is oral antidiabetic drug diabetes mellitus is one such metabolic disorder that obstruct normal step of wound healing process. Many pathophysiology study show long term inflammatory phages in diabetes wound that reduce the mature granulation tissue and parallel reduction in wound tensile strength. Due to type 2 diabetes mellitus the older patients who suffering from it having difficulty in healing process. That form complication in diabetes mellitus include ischemia and neuropathy which may lead to foot ulceration(4). For this reason is to manage diabetic wound effectively. The recently metformin hcl have been shown a number of beneficial effectto wound healing. Metformin hcl have hemostasis,proliferation ,inflammation,remodeling effect that could affect the wound healing or the risk of wound complication after surgery or injury (2,5). the objective of present study was to develop formulation of metformin hcl gel the prepare gel were evaluated for the physical appearance, homogeneity, spread ability ,PH ,and drug release through a standard egg membrane

Material And Method

Chemical

Metformin HCL is the(API),methyl paraben is the preservative is purchased by (sbspm college ambajogai), Glycerin ,Xanthum gum and Gaur gum is the natural gelling agent use for the gel is purchased by (sbspm college ambajogai),Triethanolamine is maintain to PH purchased by(sbspm college of ambajogai) ,Water for use of solvent .All chemical and reagent used in the study of analytical balance

Apparatus

Conical flask 50 ml, pipette 10 ml,Glass beaker 50 ml ,100 ml ,1000ml, aluminum foil tube 10 ml ,

Instruments

UV Visible spectrophotometer, Weighing balance, magnetic stirrer, homogenizer, Brookfield viscometer,USA Franz diffusion cell, Refrigerator, Incubator,Water bath and Oven.

Method

Various type of gel preparation method that is hydroalcoholic gel, hydrogel, microemulsion gel, anhydrous gel. These methods are the novel method used for the wound healing gel preparation.

Preparation of hydroalcoholic gel

The specific amount of drug are placed in methanol. (for table 1)thanxanthum gum and gaur gum are socked in mixture water; methanol: PG(4:4:2 w/w) this mixture are placed under magnetic stirrer for 10 hrs. and then add the triethanolamine to maintain the PH.(2)

Preparation of Hydrogel

The gelling agent are xantum gum and gaur gum are socked in a water for 2 hrs .the drug was added to this mixture and placed under magnetic stirrer for 10 hrs. Than PH and viscosity final adjust the triethanolamine (2).

Preparation of microemulsion gel

The specific gelling agent are are placed in stoppered flask .than add the 1ml alcohol into the flask.the mixture was stirrer for 10 min.than miceomulsion is form gel was adding in water with continuous stirring for another 10 min .and this gel are stored at room temperature for 48 hrs(2)

Peparation of anhydrous gel

The drug is dissolve in alcohol before the incorporation of glycerin and than add the gelling agent (xanmthum gum ,gaur gum)with continuous sterring for 24 hrs. using for magnetic stirrer.and prepared gel stored at room termperature(2)

Metformin HCL calibration curve

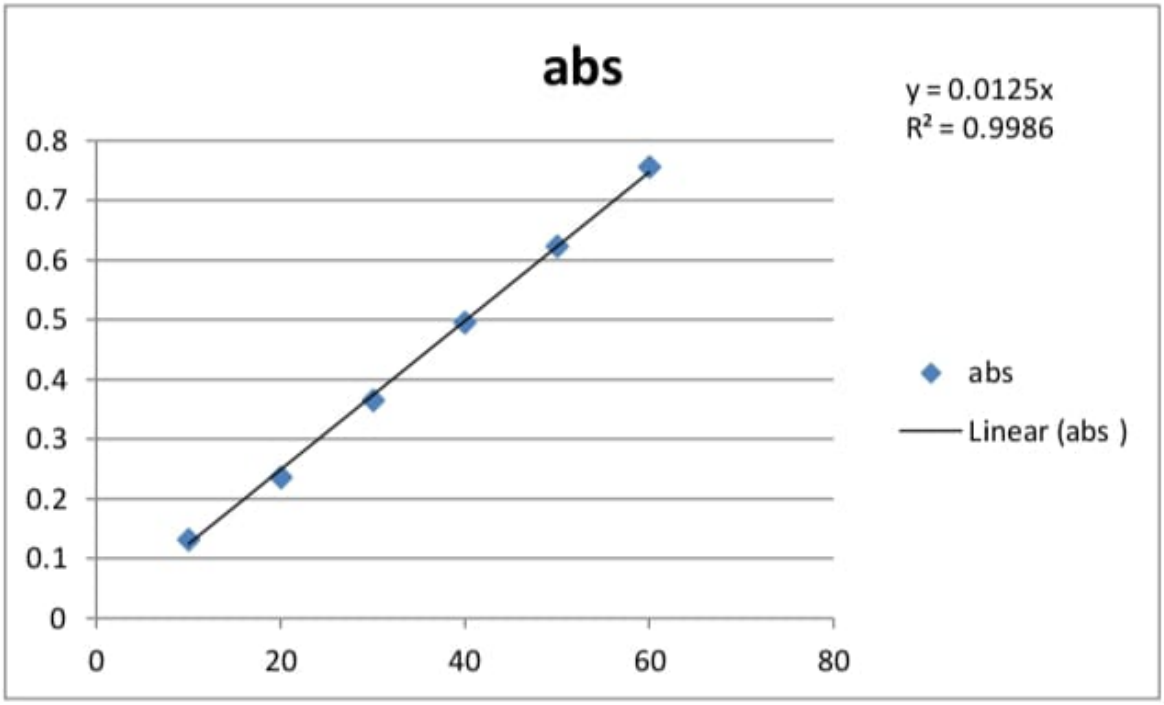

Table1:Composition of prepared gel

Sr. No.	Ingredients	Batches			
		F1	F2	F3	F4
1	Metformin HCL	0.18	0.18	0.18 gm	0.18 gm
2	Xanthium gum	0.15 gm	0.3 gm	0.6	0.3
3	Guar Gum	0.15	0.15	0.3	0.3
4	Triethanolamine	0.1	0.1	0.1	0.1
5	Methyl Paraben	0.3	0.3	0.3	0.3
6	Glycerin	0.1	0.1	0.1	0.1
7	Water	qs	qs	qs	qs

Physical Examination

The prepared gel are examine for the color, homogeneity, spared ability, PH, consistency, and microbial growth, and viscosity. The PH are measure by each sample at room temperature using digital ph. Meter. And the spread ability measure by using two horizontal plate (20cm).

Drug content studies

The 100 mg drug sample is dissolve in 100 ml of methanol .and than this solution are transfer in volumetric flask and stirring for 2 hrs at 250 rpm, than filter the solution to remove the undissolved residues and determine spectrophotometrically for the drug content.

Viscosity measurement

Viscosity measurement by Brookfield viscometer. The spindle are use Helipackt spindle set (LV-3). the spindle are rotated AT 30.0 rpm.at specific temperature for the viscosity studies of various formulation revealed that formulation f1 was better to compare to other from among all developed formulation f1 shows better drug diffusion did good rheological properties so it was concluded that formulation f1was best viscosity. Hence f1 has better result as compare to other baches.

Homogeneity

Narrow transparent glass filled with gel and observed under light to check for any lumps or practical. This are the visual observation was to find out the homogeneity.

Consistency

The consistency of the metformin in gel from which was evaluated by conical projection technique .

IN Vitro diffusion study

The semi-permeable membrane of eggs is in between the outer calcified shell and the inner contents like albumin and yolk. The shell was removed chemically by placing the eggs in 2M HCl for an overnight. This resulted in the complete decalcification of the egg and then it was washed with distilled water Carefully with a sharp pointer a hole was made on the top so that the contents squeeze out completely from the decalcified egg. The membrane was rinsed with distilled water and stored in refrigerator. The egg membrane was clamped between the donor and the receptor chamber of the Franz diffusion cell with an effective permeation area of 1.76 cm2 and a receiver cell volume of 8 mL. PBS containing 20% ethanol was used as the receptor

solution and incubated at 37 ± 0.2 °C using a water bath with a magnetic stirrer at 500 rpm. The test samples SeNP (10 mg) were added in the donor chamber. Preparation of standard solutions A stock solution is prepared using an analytical balance (1 mg/ml) that is 100 mg of pure Metformin is dissolved in 1000ml of phosphate buffer pH 6.8. Different working standard namely 5µg/ml , 10 µg/ml, 15 µg/ml, 20µg/ml and 25µg/ml was prepared by appropriate dilutions. Absorbance of those solutions is measured. (1,2,)

Calibration Curve For the calibration curve, accurately weighed of metformin was transferred to a 100 ml volumetric flask and dissolved in a mixture of buffer. From this solution, other solutions with concentrations of different µg ml were obtained by diluting adequate amounts in triplicate.

The cumulative amount of drug permeated through a unit area of skin was plotted against time. Steady state flux values (Jss) were calculated from the slope of the linear portion of the plot. The obtained Jss was then used to calculate the apparent permeability coefficient (Papp) by use of the following equation:

Papp(cm/s)=Jss/Cd, where Jss is the observed flux rate at steady-state (µg/s) and Cd (µg/ml) was concentrations of solution in donor chamber.

RESULT AND DISCUSION

Sr.no	PH	Spreadability (g/cm/s)	Homogeneity	Viscosity	Drug content (%)
1	6.6	20.80	Good	1700	98.09
2	6.5	20.83	Good	1540	99.31
3	6.3	20.70	Good	1100	99.80
4	6.5	20.75	Good	850	96.50

Table:2: Physical evaluation values for metformin HCL gel formulation

Mean cumulative percentage drug release:-

Time (min)	Absorbance	conc. (μg/ml)	Dilution factor	conc.in receptor compartment(8ml) mg	cumulative amount (mg)	cumulative amount permeated per cm sq

0	0	0	0	0	0	0
5	0.1253	10.024	100.24	0.80192	0.80192	1.4113792
10	0.1263	10.104	101.04	0.80832	1.61024	2.8340224
15	0.1275	10.2	102	0.816	2.42624	4.2701824
20	0.1365	10.92	109.2	0.8736	3.29984	5.8077184
25	0.1432	11.456	114.56	0.91648	4.21632	7.4207232
30	0.1598	12.784	127.84	1.02272	5.23904	9.2207104

Table 3: mean cumulative percentage drug release

dilution	10	
area of cell diffusion	1.76	
slope	0.0125	
flux	0.3047	
permeability coefficient	0.1713	con. Of drug taken=1gm
(flux/conc. Of drug taken)		

Jss is the observed flux rate at steady-state (ug/s) = 0.3047

Cd (ug/ml) was concentrations of solution in donor chamber = 1gm

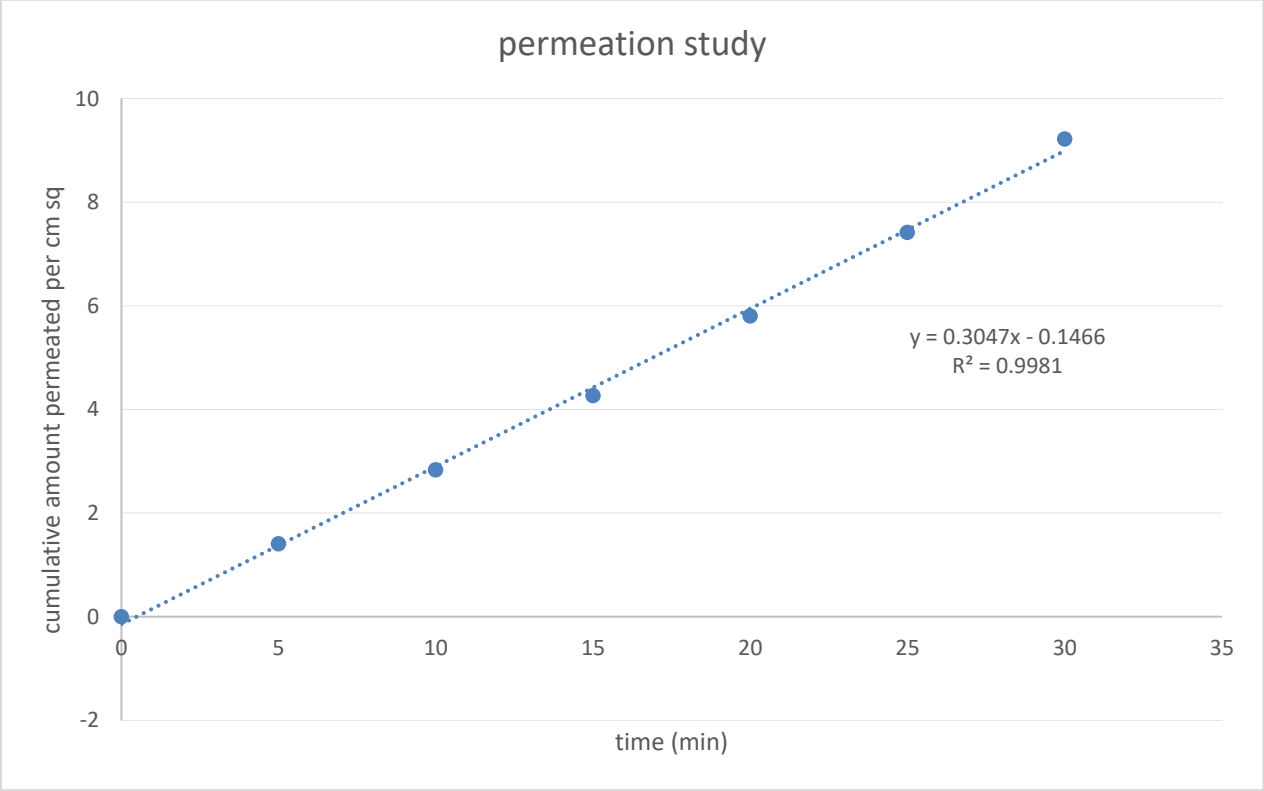

Figure: - Plots of the cumulative diffusion per cm sq

Conclusion-

In this present study and formulate for the topical gel and its properties . the gel prepared using metformin hydrochloride was found to be good gel characteristics with respect to homogeneity, sparedability, ph., viscosity, antimicrobial activity.

The result of different chemical and physical tests of gel showed that the formation could be used topically in order to protect skin damage. And their formulation for better absorption and

penetration of the active moiety into the systemic circulation in this different gelling agent can be used to formulate topical gel of metformin hydrochloride. long term stability studies as per ICH guidelines. From the above result it can be concluded that the prepared gel shows significant wound healing activity.

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